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ADDRESS OF THE PRESIDENT

MISSION ACCOMPLISHED: THE TASK AHEAD*

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IT IS MY FIRST and very agreeable duty to express to you my profound appreciation of the honor of my selection to preside over your deliberations at this, the sixty-ninth annual meeting. This accolade of surgery comes to me, I am fully conscious, not because of any personal achievement or any merit which I might possess, but as a recognition bestowed upon a representative of the surgeons of the United States who served in the armed forces during World War II.

Like many other members of this Association, I have been privileged to serve in the Army of the United States during two world wars. Because of that dual experience it is meet that I address you on the activities of the Medical Department of the Army during World War II, that I acknowledge my indebtedness to the men who helped me carry out my duties, and that, in particular, I discuss the immediate care and rehabilitation of battle casualties. All phases of their medical management were deeply and favorably influenced by the counsel and aid of almost every member of this Association, whether or not he served in uniform.

* Read before the American Surgical Association, St. Louis, Mo., April 20, 1949.

We still live in a twilight zone of tension. The world still wears the habiliments of war. The guns may be silent, but there is still no peace. Conflicting ideologies, endless irritations, unfettered national ambitions and world-wide selfishness all seem to be driving inevitably toward World War III. We still do not know whether or not there will be peace in our time. Until we know, and know beyond peradventure, we have no alternative but military preparedness, of which medical preparedness is an essential part.

THE MEDICAL PROFESSION IN THE TWO WORLD WARS

The long shadow of World War II fell across the United States long before we became active participants in it. Yet we found ourselves plunged into it with the abruptness which has characterized our entrance into most of the wars of our history. And, as has happened in other wars, the armed forces in general and the Medical Departments of the Army and Navy in particular were gravely unprepared. The explanation, of course, is simple: This is a free and democratic country, where many factors militate against preparedness and where the will of the people does not countenance, indeed is actually hostile to, a large military establishment.

Probably the most important reason, from the medical standpoint, of our perpetual unreadiness for war is that when war comes, civilian physicians must bear the entire burden of the professional services.

At the outbreak of hostilities on 7 December, 1941, there were approximately 1,200 medical officers in the Regular Army Medical Corps. Some Reserve and National Guard officers were already serving in the army that was coming into being under the Selective Service Act, but with the rapid expansion required when we entered the war more vigorous action was demanded. It was necessary, without further delay, to mobilize all physicians in these categories who were not already in service, to equip, train and allocate them, and to institute, in conjunction with other governmental agencies, procedures which would meet the future needs of the services. In World War I some 31,000 medical officers were commissioned from civilian life. Before World War II ended, approximately 60,000 medical officers had been commissioned in the Army and the Air Force and approximately 12,000 had been commissioned in the Navy. As these figures show, the response of the American medical profession to the needs of the nation was prompt and wholehearted. It recognized the task which had been placed upon it by our active participation in the war, accepted its new responsibilities, and began to reorganize the whole pattern of its professional life. One thing that it promptly perceived was that protection of the civilian health was just as large and important a problem as was the supply to the armed forces of an adequate number of medical officers to care for the sick and wounded. The dual performance was competently achieved, albeit with some of the wasteful excesses characteristic of all previous wars.

At the outbreak of World War I, as Brewer pointed out in his presidential

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address before this Association in 1920, 153 of its members, 33 of whom were Senior Fellows, volunteered for service and served in the armed forces at home, in the American Expeditionary Force in France, or in other wartime activities of the government. During World War II, when the over-all situation was so greatly changed, the response of the Association to the needs of the nation was equally praiseworthy. Fifty-eight of the membership, including six Senior Fellows, were in uniform, and practically all of the remaining members were engaged, either directly or indirectly, in some phase of military activity in medical schools and on Selective Service Boards or were participating in the war effort in some advisory capacity.

I would be remiss in my duty did I not acknowledge the debt of the Army Medical Corps to a special group of medical men, practically all of them members of this Association, the Committee on Surgery of the Division of Medical Sciences of the National Research Council. From the professional standpoint their untiring efforts and mature advice contributed inestimably to the conduct of the war. They evaluated innumerable scientific avenues of approach to medicomilitary problems, including, among others, the control of infection, the evaluation of blood and blood substitutes, the influences of various agents and processes on wound healing, the efficacy—or the lack thereof—of many methods of wound sterilization, and the value of protective armor. In addition to these specific accomplishments, and perhaps just as important, this committee stood as a stout buffer against all adventurers, the well-meaning and the fraudulent alike, who offered to the government in overwhelming numbers gadgets of various kinds and therapeutic cure-alls.

The work of this committee on the proper evaluation of agents to control infection is a service of which I would speak particularly. At the outbreak of the war the Surgeon General was placed in a real dilemma concerning the use of chemotherapeutic agents.

He received confusing advice from certain nonsurgical specialists—overly-enthusiastic—who arrogated to themselves the treatment of infections previously regarded as entirely in the province of the surgeon. His difficulty was compounded by reports, later proved to be overly-enthusiastic, concerning the efficacy of the sulfonamides at the Pearl Harbor disaster. As a result, grave mistakes were made early in the war. Later the situation was clarified, the intensive scientific studies of the Committee on Surgery and of its Subcommittee on Surgical Infections done in civilian hospitals furnishing the solid background for the military experience by which bacteriocidal and bacteriostatic drugs were relegated to their proper status, that is, adjuncts to adequate surgery.

In numerous respects a comparison of the medical aspects of World War I and World War II is instructive. American participation in World War I was short and was confined to a single theater, the European. In World War II, it extended over almost four of the six years of the conflict and four major theaters of operations were developed medically as well as militarily.

In World War I the war on the European front was static and trench warfare was the rule. Troops therefore lived underground amid unbelievably bad hygienic conditions, lack of sanitation, and exposure to disease, which probably caused more casualties than did enemy weapons. Their physical condition degenerated and recovery from wounds and infections was slow.

In World War II the advent of armored vehicles which operated in the open made for mobility on practically every front, though the disappearance of trench warfare did not prevent a tragic experience with trench foot. American troops landed in Africa, Italy, Normandy and France, and on innumerable islands in the Pacific. For the most part they were not battle-ried, but they were physically fit and they had been acclimatized to active service conditions. Along with the activity on the fighting fronts came an enormously increased fire power on the ground, through the air, and by mechanized units, a combination of circumstances which required innovations in the care of the wounded.

THE CONSULTANT SYSTEM IN WORLD WAR II

Within six weeks after the United States had entered World War II there was established in the Office of the Surgeon General a professional services division which was in sharp contrast to the prototype of this organization as it operated in World War I. In that war the consultants' division consisted of a casual group of medical men who served only part-time and who, in many instances, were not even in uniform. These civilian surgeons, many of them the most eminent in the country, were invited to the Office of the Surgeon General to advise him, sometimes on a rotating basis, sometimes merely as the needs arose, but all of them maintained their civilian responsibilities. In World War II, I think it is greatly to the credit of Surgeon Generals Magee and Kirk that the consultants in their office served in uniform throughout the war, on the sound basic concept that medicine and surgery should be practiced on a parallel to that in civilian life, namely, by specialization.

The heart of the professional program of the Army Medical Corps was the consultant service, manned by properly trained, widely experienced, and fully equipped medical men. I think it can fairly be said that this concept was fully implemented. All consultants were selected after thoughtful consideration, on the basis of their training, ability, accomplishments and professional eminence. I need not remind you how many of them, both in the Zone of the Interior and overseas, were Fellows of this Association.

When the Professional Services Division was formed in the Office of the Surgeon General, there were three major specialties, surgery, medicine and preventive medicine, represented. Later a division of neuropsychiatry was added. Consultants in the various subspecialties were then appointed, not only in the Surgeon General's Office but also in every service command in the Zone of the Interior and in the Mediterranean, European, China-Burma-India, and Pacific theaters. Here, again, comparison with World War I

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suggests itself. There was nothing like this type of organization in the service commands in this country in World War I.

In the overseas theater, however, a consultant service was developed under General J. M. T. Finney and Colonel W. L. Keller, both of them Fellows of this Association, which, had the war lasted longer, would unquestionably have expanded and operated along much the same lines as the overseas consultant services in World War II.

The function of the surgical consultants in World War II may be loosely defined as the establishment and promotion of high surgical standards by (1) formulation of policies and (2) selection and allocation of personnel. The first of these objectives obviously depended upon the second. It was immediately apparent to me upon my appointment as Chief Surgical Consultant that if the care of battle casualties and the conduct of surgical procedures were to be, in military hospitals, in the field, and in the Zone of the Interior, on the level of similar accomplishments in civilian practice, the key to success lay in the selection of properly trained personnel. Constant assessment and reassessment of the assignment of surgeons before we were actually engaged in combat and throughout the war were perhaps of greater importance and more fruitful in results than most of the other duties carried out by the Surgical Consultants Division.

The highly critical comments often made concerning the malassignment of medical officers were, I am afraid, sometimes justified from the individual point of view. In an organization which, within the space of a few months, had mushroomed from less than 1,300 men to 35 times that number, it was almost inevitable that some administrative errors should occur. I assure you, however, that whenever they were found, they were vigorously pursued by the Surgeon General's Office, and I think that on the whole they were kept to a minimum. That considerable success was achieved in the assignment of surgical personnel is evident from a survey made in 1945: A sample of 922 surgeons qualified in various specialties and serving in the Zone of the Interior showed that 96 per cent of them were doing surgery in their own fields in Army hospitals. The other 37 were serving as consultants in the nine service commands or were assigned to the Surgeon General's Office.

It was the earnest desire and consistent endeavor of the theater and Army consultants that there be a parallel disposition of specialized talent in overseas installations, and it can fairly be said that considerable success was achieved. The program of supervision, co-ordination and policy making which originated in the Surgeon General's Office and which was integrated throughout the various echelons in the Zone of the Interior and theaters of operations resulted in a remarkably equable disposition of talent and in the consequent maintenance of a standard of surgery that was always comparable, and frequently superior, to that available to a cross section of the civilian population.

The consultant system was the keystone of the arch, the essential element, of the laudable surgical record achieved by the Army Medical Corps in World

War II. I tell you nothing, however, that you do not already know when I say to you that numerous organizational difficulties attended its full implementation. For this, there were a variety of reasons: so-called bulk allotment of personnel, limitations of rank, rigidity of unit organization, and the absence of a consultant specification in Tables of Organization. Furthermore, the line of communication within the consultant system, itself, was extremely unsatisfactory. Since the consultants were essentially advisors, without command responsibilities, they should have had what they never had, a clear line of communication within their own system, organizationally pyramidal in structure and converging at the summit in the person of the chief consultant. Within such a system, had it existed, technical control could have flowed down peripherally, flexibility of movement would have been possible, coordination of activity would have been encouraged, exchange of information would have been prompted, and the whole system of operation would have been more effective.

The relationship of the consulting surgeon to an army or a theater or a service-command necessarily revolved around his relations with the line. A medical officer, regardless of his rank, always had to keep in mind the important fact that he was an advisor and had to remain an advisor. His opinions, properly, had to be subordinated to the tactical situation. Yet despite these restrictions it was his duty to express his opinion firmly, fearlessly and tactfully. It was his duty to raise his voice although none knew better than he that all too often, like the Prophet of Israel, his was a "voice crying in the wilderness." His opinions on important and frequently vital professional subjects were usually accepted, were occasionally rejected, and were almost always modified. Frustration, in short, was likely to be the lot of a medical officer, regardless of the echelon in which he served.

THE CONSULTANT SYSTEM IN OVERSEAS THEATERS OF OPERATION

Let us examine, for a moment, the work of the consultant system in overseas theaters of operations in World War II. In the Pacific Theater the consultant system came into being late and was never fully implemented, partly because of the shortage of personnel and partly because of the deliberate postponement of a major effort in that area until the conclusion of the European phase of the war.

In the Mediterranean Theater, which served somewhat as a proving ground for future medical activities, the operation was confined to, and was executed by, a single army, the Fifth, whose maximum strength was eight American divisions. The operation was both holding and assault in character. The medical personnel was probably the best ever supplied to an army operating in the field. The professional care of battle casualties was excellent.

The European Theater of Operation was recognized by one and all as the major theater of the war. The fighting was primarily offensive. The more than 70 American divisions, together with the numerous Allied divisions which

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participated in the assault, were held together in Army Groups instead of single armies. In this theater the care of the wounded was handled admirably due in large measure to the indomitable spirit and remarkable personality of the late General Elliott C. Cutler. The liaison which he established with the American Command and with British and French surgeons was unusually happy. The result of his efforts was the surpassingly good care which our battle casualties received.

The successes of the consultant system in the major theaters of operations, as well as in the Zone of the Interior, were personal triumphs for the consultants. They refused to be shackled by the circumstances under which they had to work, and the outcome was happy and desirable. We would do well to remember, however, that had they been men of different personalities, men of less professional and moral courage, the outcome might well have been different and the medical care of battle casualties might well have been seriously handicapped.

All surgical consultants in overseas theaters functioned with extreme effectiveness, but they had to rise above the system to do it. They had to overcome the limitations of authority and the difficulties introduced by the subordination of the Army Medical Corps, a professional service to a Service of Supply which dealt in commodities and in nonprofessional services.

SPECIALIZATION IN THE Z I

The administration of the surgical specialties in the Zone of the Interior differed from their administration in zones of combat only in the number of personnel employed under changing conditions. I acknowledge my obligation to the consultants who worked in the United States during the war. They carried out manifold duties and bore heavy responsibilities. If, however, I were asked to name their greatest achievement I would say, without hesitation, that it was the establishment of specialized surgical centers in the general hospitals. These centers, which clearly reflected the Surgeon General's desire to foster specialized surgical care, represented an innovation in the professional services of the Army.

As time passed, there were created six amputation centers, 21 neurosurgical centers, five thoracic surgery centers, three vascular surgery centers, eight plastic surgery centers, eight centers for ophthalmologic surgery, two centers for the rehabilitation of the blind, and three centers for the rehabilitation of the deaf. These installations were provided with the most modern general and specialized technical equipment required in each field. More important, they were staffed by men who were highly competent in their specialties and whose time and effort could be used to the fullest advantage, and with a minimum of waste, because their patients were concentrated. I do not exaggerate when I say that many casualties, who in earlier wars would have remained casualties forever, were restored to useful and productive lives.

These centers served a further purpose. They afforded an opportunity for on-the-job training to young surgeons whose residencies and apprenticeships had been interrupted by the war. For obvious reasons, nothing approaching the complete training afforded by civilian teaching hospitals in peacetime could be undertaken in these centers, if only because the pressure of work would not permit it. But it is not too much to say that the training program which was carried out under civilian specialists in uniform compared very favorably with its counterpart in civilian practice. The specialty boards accepted that point of view when they decided to grant credits for it in their requirements for certification.

The training program in neurosurgery is perhaps the best illustration of this achievement. It was undertaken as a matter of sheer necessity. When, in February, 1942, we began to mobilize specialized talent for the care of our armies overseas and at home we were astounded to discover that in the whole United States there were only 154 certified neurosurgeons. The significance of that number did not become fully apparent, however, until we found that to meet the Tables of Organization of Army hospitals it would be necessary to strip every civilian clinic of its neurosurgical personnel. And even then the Army would have been left short.

Army needs had to be met. Something has to be left for civilian needs. The most practical solution was to train young general surgeons, as quickly as possible, in the essentials of neurosurgery. A program of instruction was therefore set up, the first part consisting of didactic lectures and anatomic dissections, the second part of clinical training in neurosurgical centers in the United States. In these centers, by lectures, ward rounds, work in the operating theater, and ward work, the young surgeons who had completed their didactic and theoretical training were taught the practical aspects of traumatic neurosurgery. In all, some 200 young general surgeons were thus trained, and the exceptionally fine service which they rendered overseas and at home is the background for the unprecedentedly good care which neurosurgical casualties received in World War II. Without this training program it could not possibly have been accomplished.

To my mind, this demonstration of the possibility of rapid training of specialists in an emergency is one of the major medical accomplishments of World War II. If it proved applicable to the training of neurosurgeons in time of war, it should be equally applicable to the training of other surgical specialists in any other emergency. That is a significant possibility from the military point of view, but it has its lessons for civilians as well. In the pre-war years there was a decided tendency in all the surgical specialties, including neurosurgery, to underestimate, and even to belittle, the value of a sound background in general surgery. The war experience makes it possible to say flatly that this sort of background is highly important in the training of all surgical specialists, and that in time of war the possession of such a background is almost essential.

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THE CLINICAL ACCOMPLISHMENTS OF WORLD WAR II

Mortality. In each major war for which statistics are available, beginning with the Peninsular Wars, the death rate of the preceding war has been halved. The improvement in World War II was even greater, the percentage of men dying of wounds being 3.3, as compared with 8.1 in World War I. In wounds of the most potentially lethal portions of the body, that is, the head, chest and abdomen, the mortality rates in World War II were almost 65 per cent lower than similar rates in World War I. This is a gain that is worthy of high praise, though the unhappy realization remains that had we learned many of our lessons earlier in World War II, we might have saved many more lives. I make that statement soberly, with full consciousness that World War II lasted much longer than World War I, that it was fought over different types of terrain, and that it was fought with far more lethal weapons.

The four factors which most vitally influenced the mortality and morbidity rates for battle injuries in World War II were:

1. The availability of a large number of excellently trained young surgeons, who could be placed well forward in combat areas.

2. Improved methods of resuscitation, including, among other things, the lavish use of blood and blood plasma. This improvement underlay success in all fields of surgery in World War II, and it would be impossible to speak of it without making special mention of Colonel Henry K. Beecher. To him goes the credit for the pattern of resuscitation developed in the Fifth Army and advantageously followed throughout the rest of the war by all other Army elements. His concept of resuscitation and its able implementation resulted in delivering to the surgeon a patient who, in spite of the circumstances of battle, always presented a better risk than he had presented when he was brought off the field and who frequently presented an optimum risk.

3. The control of infection by antibiotics and chemotherapeutic agents which, it should be emphasized once more, were properly used only as adjuncts to surgery.

4. Improved transportation facilities and, in particular, transportation by air, which permitted rapid evacuation from forward positions all the way to the Zone of the Interior.

Upon these factors and their ancillary ramifications rested the hopes of the surgical program. The ultimate evaluation of the care of battle casualties and the marked lowering in the general and special mortality rates amply testify to the competence with which they were applied.

The Management of Wounds. It would be difficult to challenge the assertion that no epoch-making discoveries came out of World War II in respect to the treatment of battle wounds. Old principles employed in past wars were modified and surgical progress was forwarded by many ingenious innovations, but nothing really new came into existence. The three stages of wound management, namely, early and complete debridement, delayed (so-called sec-

ondary) wound closure, and reconstructive surgery, were exactly similar to the principles employed in World War I. They were modified and refined in practice, with infinite advantage to the wounded soldier, but as principles they remained unchanged.

Debridement was done close to the front line. Transportation facilities permitted rapid evacuation to hospitals far to the rear, or, in the European Theater, to England, for the second phase of the program. Practically all of the reconstructive surgery was done in hospitals in the Zone of the Interior.

The debridement of war wounds had its beginning in principle under Desault and his pupil Larrey, Napoleon's Army surgeon, who was unquestionably one of the great military surgeons of all time. The exact meaning of the term, however, has somewhat altered over the years. Desault and Larrey described debridement as a deep incision for the purpose of exposing the anatomic structures and exploring and draining the wound, but Desault believed, as the surgeons of World War II learned if they did not already know, that the excision of dead tissue was the more important part of the procedure.

Recent usage has made the term debridement synonymous with excision or revision of the wound, but there was so little difference between the principles and practice of this operation as it was performed in World War I and in World War II that Pool's article on the subject published in 1919 might equally well have been published after the second World War.

After debridement, however, the surgeons of World War II had an enormous advantage over the surgeons of World War I. In the late war there were available extraordinarily efficacious sterilizing agents which controlled infection, even of the gravest kind. Gas infection, which had been so frequent in World War I, was conspicuously infrequent in World War II, partly because of prompt operation and satisfactory transportation facilities, partly because of the more favorable terrain over which the fighting was done, and in large part because of the use of chemotherapeutic and antibiotic agents, which, although they perhaps had little if any effect upon gas-producing organisms, were definitely inhibitory to symbiotic bacteria. When one recalls that sterilization of wounds in World War I was chiefly confined to the utilization of the cumbersome and inconvenient Carrel-Dakin technic, one is able to appreciate more fully the striking changes in the picture.

One of the surgical lessons which was really learned well in World War I was that primary wound closure was disadvantageous and actually contraindicated. It had an extensive trial and it was finally given up, except under ideal conditions. Early secondary closure, or delayed closure as we called it in World War I—a difference only in nomenclature—was practiced by Heuer, Pool and others at Evacuation Hospital I at Sebastopol, France, and Rene LeMaitre and DePage both recorded gratifying end-results in large numbers of cases handled by this method. The interval between debridement and wound closure varied from one day to six to ten days, depending upon local

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conditions and depending also upon the bacteriologic findings, which then furnished the chief criterion for the decision.

In World War II clinical criteria were largely substituted for bacteriologic criteria and proved entirely reliable. It is safe to assume that the properly conducted second stage of wound management in the base area, following a properly conducted debridement in the forward area, was at the heart of the very satisfactory mortality and morbidity statistics of the second World War.

Wounds of the Extremities. Wounds of the extremities have always constituted a major proportion of all wounds in all wars. In World War II they made up approximately 83 per cent of all battle-incurred wounds. The number was increased first by the large numbers of fractures which occurred during the training period and second by the conversion of the Army to motor transportation and by the utilization of tanks in battle. I do not have the exact statistics, but it is my own belief that the fractures incurred in training programs, maneuvers and similar activities equalled, or perhaps exceeded, the number incurred by enemy action.

The picture of wounds of the extremities in World War II, as in all wars, was complicated by the frequent association of fractures with wounds of the soft parts and of blood vessels and nerves. The association was more frequent in this conflict than it had been in previous wars because of the high fire power of both artillery and bombs from the air, which had a wide range of devastation and which were far more damaging than similar agents used in World War I, when some sort of protection was possible against known shell trajectories.

The management of compound fractures in World War II showed remarkable improvement in the technical phases of management in forward hospitals and in the broad application of such procedures as early secondary closure or delayed internal fixation of mal-aligned compound fractures in base hospitals. The general concept, which was essentially sound, was that an injury to a bone should be treated on exactly the same surgical principles as an injury to any other tissue of the body. Furthermore, the program of management was predicated on the fact that all battle fractures must be regarded as septic, partly because they were usually associated with extensive damage to the soft parts and partly because they were so often received under conditions favorable to the introduction of foreign bodies and bacteria.

The program of management of compound fractures in their early stages was admirably summed up by Hampton. The spotlight, he noted, was removed from bacterial flora to the pathology of the open wound, and the surgical program was based on excision of dead tissue, whenever and wherever it was found; obliteration of dead space, or its dependent drainage; staged closure of the wound; atraumatic technic, with fine hemostats and ligatures; pressure dressings; adequate reduction and immobilization of fractures; precise splinting; and the adjuvant use of penicillin and whole blood.

These surgical principles were learned early in the war, in the North African-Mediterranean Theater. When they were applied to the large numbers of compound fractures received in the Normandy landings and elsewhere in the European Theater, and when they were supplemented by the great reduction in the time lag brought about by improved transportation facilities, the soundness of the new program of management was irrevocably affirmed.

Nerve Injuries. Contrary to pre-war predictions, nerve injuries constituted nearly 10 per cent of all battle casualties in World War II. In numbers, in seriousness, and in the duration of the necessary treatment the neurosurgical was second only to the orthopedic load. It is still impossible, and perhaps never will be possible, to determine accurately the number of these wounds. I think it likely that the overall figure will be close to 100,000.

The management of a neurosurgical load of this size was a colossal task which was brilliantly initiated in the European Theater by Colonel Loyal Davis. When he returned to the States because of ill health, he was succeeded by Colonel R. Glen Spurling who carried the program through to a successful completion. Colonel Spurling then returned to the States as Consultant in Neurosurgery in the Office of the Surgeon General and in cooperation with Colonel Barnes Woodhall was responsible for the program in the neurosurgical centers which was so vitally important.

The collaboration and wise counsel of Dr. Jason Mixter, who served as Civilian Consultant in Neurosurgery to the Surgeon General's Office, is gratefully acknowledged as a fine contribution to the war effort.

The details of the highly successful neurosurgical methods used in World War II have already been recorded in detail in the literature and need no repetition. I would like, however, to comment briefly on three major categories of neurosurgical casualties, head injuries, peripheral nerve injuries, and injuries of the spinal cord.

The management of acute penetrating wounds of the brain in World War II followed with no essential modifications the basic concepts formulated by the late and great Harvey Cushing for the management of similar injuries in World War I. The neurosurgeons of World War II, however, unlike those of World War I, had almost perfect control of the infection which so often turned success to failure in the earlier war. Thanks to the sulfonamides, and later to penicillin, to liberal supplies of blood and plasma, and to rapid evacuation by air, Cushing's original principles were adapted to military circumstances in the second World War in a fashion which even that brilliant surgeon, with his imaginative outlook on neurosurgical problems, would not have dreamed possible in 1917 and 1918.

Perhaps the most important thing the neurosurgeons learned about head trauma in World War I—it was proved amply again in World War II—was that, unless the patient's condition were deteriorating, it was not necessary to hurry him into an emergency operation. He was, in fact, better for a delay which permitted adequate resuscitation and also permitted operation under an

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optimum environment. This policy reduced morbidity and prevented mortality. It also had practical advantages for other wounded men. The front line surgeons, with a clear conscience, could send patients with head injuries to the rear while they busied themselves with urgent cases in which delay could not be tolerated and while, in addition, they kept beds in the forward zone clear for urgent casualties.

In one respect the most significant contribution made by Army neurosurgeons during World War II had to do with peripheral nerve injuries, since they constitute a problem which can be solved only in time of war. In World War I the same opportunity existed but it was lost because no accurate or comprehensive follow-up studies were made. In World War II that error was avoided. Early in 1944 a Peripheral Nerve Registry was set up in the Surgeon General's Office, in which, by the end of the war, more than 8,000 peripheral nerve injuries had been entered. Several interim analyses have already been made, and when, at the close of the appointed five-year period, the final analysis has been completed, the results of peripheral nerve surgery in World War II will be unequivocally clear and the pattern will be established for the proper management of similar civilian injuries.

An extremely important, and certainly the most humane and dramatic, development in military neurosurgery in World War II was the program for the care and rehabilitation of soldiers with injuries of the spinal cord. These casualties, in the acute phases of their injuries, were primarily neurosurgical problems and the neurosurgeons saw to it that every man with a penetrating wound of the spine had the benefit of prompt surgical exploration by experienced personnel. Neurosurgeons, furthermore, worked unceasingly to expedite the transportation of these patients from forward hospitals to rear echelon installations adequately equipped for their treatment. The transportation of casualties with spinal cord injuries, as I need not remind you, is a chapter of achievement in itself.

I do not hesitate to assert that the reason so many of these tragically wounded men are alive today and are rehabilitated is the faithful and unremitting endeavor of all concerned in their care, beginning with the neurosurgeons, to supply prompt and expert treatment to them in the first phases of their injuries. As soon as possible after initial surgery paraplegic casualties were evacuated to one or another of the 21 paraplegic centers in the Zone of the Interior. Here a rehabilitation program was begun, based on the well recognized policies which had proved their effectiveness in civilian clinics but which were applied in the Army centers with an efficiency and zeal and sympathetic understanding that far surpassed any previous effort. Great credit for the success of the program belongs to the individual urologists, orthopedic surgeons, rehabilitation and dietary experts, physical therapists and other specialists who shared with the neurosurgeons the responsibility for it. Even more credit belongs to them as a group, for they provided an example of wholehearted, efficient medical and surgical cooperation that is unique in Army and

civilian practice alike. I think they have had their reward. The ultimate goal of the Army paraplegic program was to enable every such casualty to resume his former place in civilian life. It is a source of happiness and satisfaction to all who participated in the effort to realize that that goal has been achieved beyond what any of us dared to hope.

Vascular Injuries. The number of patients with vascular injuries received in the Zone of the Interior from the combat areas so far exceeded all expectations that the establishment of centers for their specialized care was almost inevitable. The vascular center at Ashford General Hospital, which logically was headed by Colonel Daniel C. Elkin, with his long-time interest in vascular and cardiac injuries, served as a sort of pilot plant for the centers at Mayo General Hospital, under the direction of Colonel Harris B. Shumacker, Jr., and at DeWitt General Hospital, under the direction of Colonel Norman E. Freeman. The astonishingly low mortality achieved in these centers—four deaths in 803 operations for aneurysm and arteriovenous fistula, for instance—and the equally remarkable functional results, are all the testimony one needs as to the wisdom of the policies adopted in this field of surgery.

It ought to be emphasized that far more than vascular injuries became the business of the vascular centers. Well over a thousand patients with cold injuries, chiefly trench foot, were treated at the Ashford Center alone, and all three centers have to their credit a brilliant record of treatment of this condition, a record which counterbalances, so far as that is possible, the unhappy record of its prevention, or, more correctly, of the failure to prevent it. I need not remind you that the incidence of trench foot in the Mediterranean and European Theaters is one of the blots on the Army record in World War II, though I feel perfectly justified in adding that if the warnings of the Surgical Consultants Division had been heeded by Command the record would have been quite different.

A significant and important phase of the work of the vascular centers was the investigative program carried out, in one form or another, at each of them. The clinical and physiologic studies which were made will be of lasting usefulness in the management of civilian vascular diseases. As the result of these investigations, many of the problems in this field which had hitherto been unsolved, or the solution of which had been based on little more than speculation and presumption, were solved or are well on their way to solution.

Equally important are the follow-up studies now being carried out under the direction of the National Research Council and with the cooperation of the Veterans Administration. The critical evaluation of late results is of greater worth because of the continuous detailed observations made upon these men from the time of injury.

I have little doubt that these various studies will remain one of the largest and most successful contributions which will ever be made to the knowledge of the pathologic physiology of vascular injuries and of their management.

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Abdominal Injuries. Abdominal wounds are always the most serious of battle injuries because they are seldom simple. It is the exceptional case in which only a single viscus is injured. Wounds of the small intestine are almost always multiple and are frequently associated with damage to the large intestine and to the bladder, kidney and spleen. Moreover, 10 per cent or more of all abdominal wounds are abdominothoracic, a variety which is far more serious and more difficult to manage than wounds confined to the abdomen.

These generalizations all apply to the abdominal injuries encountered in World War II, and it is therefore pleasant to be able to report that while the mortality for these wounds in World War I was between 60 and 75 per cent, in World War II it was reduced to between 25 and 35 per cent, although the percentage of operability was the same in both conflicts. The improvement is clear proof of what earlier surgery and better methods of resuscitation can accomplish.

As to methods, no outstanding changes in technic were developed in World War II, though it did become routine to exteriorize all wounds of the colon, except those of the cecum and ascending colon, which could be handled, like wounds of the small intestine, by primary suture. It also became routine to perform colostomy in all wounds of the rectum, with a considerable improvement in results because the diversion of the fecal stream reduced the amount of infection.

Early in the war it was customary to introduce sulfonamides into the peritoneal cavity in all abdominal wounds. This method was soon found to be fraught with considerable danger of adhesions and of intestinal obstruction, and it was abandoned by order later in the war.

Damage to the kidney and spleen usually called for splenectomy and nephrectomy. Wounds of the liver were rapidly fatal in a high proportion of cases, though at that, a surprising number of lives were saved by immediate operation. The control of hemorrhage was the immediate objective of laparotomy, which was performed whenever the casualty survived long enough to permit it, for enormous damage was done to the parenchyma of the liver, especially if the missile had been fired at short range.

The mortality of abdominal wounds is difficult to evaluate and statistics are frequently misleading because of the multiplicity of wounds and the circumstances of wounding. There is no doubt, however, that the lives saved in this type of injury in World War II can be attributed to adherence to the principles just outlined and to a postoperative regimen in which skilled nursing care was supplemented by nasogastric suction, chemotherapy and antibiotic therapy, the lavish use of blood, and the correction of protein and vitamin deficits.

Thoracic Surgery. The first substantial advances in the field of thoracic surgery, regardless of the lesion, occurred in World War I. In the interim between the wars important contributions from various surgical clinics all over the world established the feasibility of this branch of surgery, and World

War II furnished an enormous clinical laboratory in which to test old and new concepts.

The final statistics on injuries of the chest in World War II are still to be compiled, but it is safe to say that they will prove considerably lower than in any previous war. In 1944 Carter and DeBakey reported a mortality rate of 8.1 per cent in more than 20,000 chest wounds treated up to that time, against a mortality for similar injuries in World War I of 24.5 per cent.

It is tempting to attribute these results to the adoption of new and radical operative procedures perfected between the two world wars, but it would not be true. Actually, lobectomy, pneumonectomy and other radical thoracic operations found little place in the treatment of wounded men. Refinements in surgical technic and the availability of chemotherapeutic and antibiotic agents and of large supplies of blood had much to do with increasing survival rates. More important were the judicious timing and the proper selection of surgical procedures, and still more important were adequate resuscitative measures. No patient was operated on until shock was controlled and his condition was stabilized. There was full appreciation, moreover, of a feature peculiar to chest wounds, that partial suffocation can be a major factor in producing shock when intrathoracic structures are injured. It was soon discovered that a rapidly fatal outcome could be expected if accumulations of blood or mucus in the trachea or bronchi were not promptly removed by catheter suction or bronchoscopy. The so-called wet lung was an even more serious problem, for which the liberal administration of oxygen furnished the best solution.

In World War II the chief emphasis was placed on the status of the intrathoracic organs. Less attention was paid to the thoracic wall, unless an open sucking wound was present, when, of course, immediate closure was carried out. Another important consideration in respect to the chest wall was the control of pain originating in it from fractures or other injuries. Injections of procaine at the site of the injury were effective, and paravertebral block gave even better results. These simple measures were far more important than they might seem, since the control of chest pain played a major role in the management of shock in thoracic wounds and since the strapping ordinarily used for such lesions in civilian life was found to cause a dangerous reduction in vital capacity when it was employed in casualties with extensive chest wounds.

Another lesson learned from the recent military experience was that the conservative management of hemothorax practiced in civilian life has no place in the management of severe battle-incurred thoracic injuries. The idea that the early evacuation of blood from the pleura was not only not necessary but might result in secondary hemorrhage was quickly overturned. The prompt evacuation of the hemothorax, without air-replacement, permitted the re-expanded lung to occupy the pleural space, and if empyema did occur, it was practically always of small volume. Failure to evacuate the hemothorax, how-

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ever, was likely to be followed by the development of a chronic hemothorax or fibrothorax and by later secondary infection.

For many years after World War I the wards of Army hospitals were filled with respiratory cripples. Some of them were suffering from pyogenic empyema secondary to pneumonia, but many others could thank the ultraconservative treatment of traumatic hemothorax for their condition. We are not witnessing any such unhappy situation today. Chronic empyema was actually rare in World War II. Antibiotics and chemotherapeutic agents controlled pyogenic empyema, the proper surgical management of traumatic hemothorax practically eliminated serious chronic pleural abscesses, and decortication of the lung, as revived by Burford and others, took care of clotted hemothorax. The ultimate objective of the management of hemothorax was early, complete re-expansion of the lung, with conservation of as much cardiopulmonary function as possible. It was achieved in a truly remarkable number of cases.

A word must also be said about the large number of thoracic lesions observed in World War II which were not of combat origin. Thousands of cases of bronchiectasis were seen, most of them not related to chest wounds. Many of them were treated by surgical extirpation of the diseased lung tissue. The remarkable accomplishment of Meade, Kay and Hughes, who performed 196 lobectomies, chiefly for bronchiectasis, with only one death, at the Kennedy General Hospital Thoracic Surgery Center, was more or less duplicated at the other thoracic centers.

Intrathoracic tumors, which were also discovered in surprisingly large numbers, were treated earlier than in any comparable series in civilian life, because routine roentgenograms of the chest were made when the soldier was inducted into the Army and again when he was ready for discharge. Regrettably, many of the cases of bronchiogenic carcinoma discovered, usually by accident, in these young men were inoperable. On the other hand, the results in mediastinal tumors were extremely encouraging. Blades, for example, reported 109 cases at five Army hospitals over a three-year period without a single surgical death in the resectable lesions.

It must be borne in mind, before we congratulate ourselves too heartily on the dramatic advances in thoracic surgery during World War II that the subjects of the operations, whether they were performed for wounds or for diseases of the chest, were usually young men, and, more important, young men who had not withstood the ravages of chronic pulmonary disease. We can scarcely expect that the lower mortality rate achieved in this group can be duplicated in civilian life, in which thoracic surgery is chiefly performed in an older age group, with advanced disease. The lessons learned in the care of severely wounded soldiers, however, and the experiences gained during the war in surgical diseases of the chest, have furnished information which will be invaluable when it is applied, as most of it can be, to the management of diseases and injuries of the chest in the civilian population.

The organization of the thoracic centers in the Z I was directed by Colonel

Brian Blades whose sound advice to the Office of the Chief Consultant in Surgery was invaluable and to whom I make a sincere acknowledgment of my appreciation.

Plastic Surgery. In the 300-page record of plastic surgery in World War I, skin grafting is mentioned in a single sentence. Burns are not mentioned at all. In World War II at least a third of the work in plastic surgery concerned free skin grafts, and about a third of it was carried out for burns.

It must be granted, however, that modern plastic surgery received its first real impetus in World War I and that the lessons learned in the course of it were later transferred to civilian use. In all probability the evolution of the management of burns can be attributed to the results achieved in the Coconut Grove disaster in Boston in December, 1941, shortly after the United States had entered World War II. The sound conclusions drawn by the men who treated those casualties formed the background of the management of burns in the second World War, when the increased use of combat motor vehicles, both on land and in the air, made the care of these casualties a serious problem clinically, while the numbers of casualties with these injuries required their management on a mass basis.

We were greatly assisted, in setting up the plastic surgery program, by Dr. Jerome Webster, Dr. Robert Ivy, and the late Dr. John Staige Davis, who gave unsparingly of their time and effort and who responded to every call. To Colonel James Barrett Brown, however, belongs more than to anyone else the credit for what American plastic surgeons achieved in World War II. In 1942 he was ordered to the European Theater, to study the casualties which had occurred as the result of the brief struggle on the Continent and the continuing blitz warfare.

When he returned, he served both as chief of the plastic service at Valley Forge General Hospital, the first of the plastic centers to be established, and as advisor in plastic surgery to the Chief Surgical Consultant in the Office of the Surgeon General.

But tribute must also be paid to all the other plastic surgeons. They performed some 40,000 operations without a death. They were always numerically in short supply, but they carried an enormous burden of work—at one time 33,000 operations were scheduled for performance on the 11,000 patients then in the eight plastic surgery centers in the Zone of the Interior. Many of these highly skilled surgeons had to be kept in the Army for a year or more longer than their associates, long after they could have been released on points, because the work they were doing could be done by no one else.

When I asked Colonel Brown to outline for me what he considered the highlights of his specialty as it was practiced in World War II, he listed the following points:

1. The elimination of tannic acid in the management of burns and the substitution of atraumatic care of the wound, the use of pressure dressings to prevent loss of serum, and early skin grafting.

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2. The early closure of wounds, either by grafting or by suture, with or without the utilization of flaps.

3. The establishment of specialized centers and of specialized teams in the combat zone for the immediate care of casualties suffering from burns and facial injuries. The superior functioning of these services cut down very materially the time required for the definitive and long-drawn-out plastic repairs to be done in the Zone of the Interior.

4. The extensive use of local tissue in repairs.

5. The fundamental principle of wound closure, which was highly developed by plastic surgeons and which was used in many cases preliminary to secondary orthopedic or neurosurgical procedures on the deeper tissues.

6. The concept that deep healing can be no better than superficial healing.

7. The close cooperation of plastic surgeons with dentists, anesthetists, orthopedic surgeons, neurosurgeons and the nursing service in the management of their casualties.

8. Special procedures devised for the management of injuries in particular regions, including the palate, the jaw, the nose, the ear and other parts of the face, the lower extremities and the hands.

As Colonel Brown well expressed it, the miracles of reconstruction performed by the plastic surgeons would have been impossible without the courage and the will to live displayed by these young men who seemingly had been marred for life, and without the industry and confident hope of the surgeons who restored them to lives of useful activity. Medical history has no finer example of the doctor-patient relationship, and plastic surgeons have every right to be inordinately proud of what they accomplished.

LOOKING FORWARD

As one looks to the future, the conclusion seems inevitable that if war comes the menace of the atomic bomb plus the addition of new technics will make it a more horrible and devastating conflict than any which has preceded it. It will bring into the zone of destruction all civilians as well as members of the military establishment.

The introduction of atomic weapons wipes out many of the old concepts of war, erases zones of security, and makes combat truly global. A declaration of war would be followed immediately by a huge number of casualties, largely civilian, such as no battle between military forces has ever produced.

"We shall be left literally with 'No Place to Hide,'" as Bradley has said in his remarkable book of that title. "Bikini," he points out, "is not merely a ravaged and useless little atoll in the deep far Pacific. Bikini is our world."

War would require the immediate and rapidly complete mobilization of the entire medical personnel of the nation on a disaster basis and indeed should require a mobilization of our entire citizenry, a step imitating totalitarian methods but definitely necessary and I believe certain to be invoked when and if combat fully develops.

It must be recognized that as war develops air power takes an increasingly prominent part, and while it may be argued by the military that the atomic bomb has not greatly changed basic military principles nor obviated many of the conventional roles of military forces, supersonic planes, guided missiles, and radar controlled guns guarantee an immediate scope of action and a destruction of both humans and war potentials never before dreamed of. Air attacks will be followed by invasions and counter-invasions; the ensuing warfare, we are told by Groves, will then be orthodox in principle but not in detail. The Army still insists that all efforts of the military team are for the breaking of the enemy's resistance and the final advance of ground troops onto enemy soil. Naturally such widespread operations, so devastating in character, so unorthodox in execution, will call for leadership both in the field and in the rear echelons far greater than in the past.

To the end that some plans be formulated and some attempts be made to avoid the almost complete absence of medical plans such as happened in World War II, it is essential that the medical profession coordinate its efforts and assume leadership for an over-all plan. Certainly the armed forces branches snarling at each other and grasping to forward each its own department are ill-fitted for and incapable of this over-all planning. Clemenceau is said to have remarked that war was too serious a business to be left entirely to the military. Perhaps he meant to intimate that the politicians were more able to meet the inevitable problems of conflict. He must have known that Clausewitz defined war as the employment of organized violence to obtain political goals.

All this is to say that civilian agencies will and should dominate the direction of all efforts, certainly at the beginning of another conflict. From the medical standpoint the military must be properly supplied with doctors but, and I emphasize this, only after a proper integration with civilian needs and resources. This overwhelming responsibility should be apparent, I think, to all medical men and I deprecate the laissez-faire attitude which seems to pervade our country at the present time. True, the military establishment is making efforts to put into effect some of the concepts thrust upon it in the recent war, but the process is slow and fitted only for the military establishment itself.

The changing pattern of warfare of World War II developed a new military philosophy whereby the major efforts of destruction were aimed at war making potentials and particularly industrial resources. This change out-modes the modern army's Tables of Organization in so far as medical troops are concerned.

The Council on National Emergency Service of the American Medical Association has advocated two developments within the Defense Establishment. The first is "a permanent board of top flight civilian physicians working arm in arm with the Surgeon Generals at high enough level within the military establishment to supersede the uninformed and often arbitrary authority of command." The second is "a group of civilian physicians at top level within

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government having the responsibility of weighing the medical man power needs of industry, agriculture and the civilian population at large, of research, public health work and medical education against the requirements of the military establishment."

Such planning is all very well but I venture to question its practicability. I see no particular advantage in going "arm in arm" with the Surgeon Generals of the armed forces until they are given authority in medical matters which is now exercised by officers of the Service of Supply and of the line.

Also, within a few months the Voorhees Report published by the Hoover Commission has been made available to the public and it is worthy of careful scrutiny and consideration by all medical men. It reflects mature judgment and sets down on paper recommendations which are so sound, so saving of personnel, materiel, and funds that it is easy to join in the fervent hope of its adoption in large part.

It is a long step in the right direction but it applies to federal agencies only, including the armed services, whereas coverage of the entire population is demanded. Obviously this calls for planning on a high level and with authority. As of today there are no plans and there is no authority. The problems which will confront medicine in the future, and particularly war medicine, will be overwhelmingly greater than those of World War II.

The introduction of atomic weapons may possibly change the entire concept of the surgery of trauma. It certainly will introduce new problems for the treatment of irradiation, blast injuries and burns. It will call for an entirely different type of cooperation between military and civilian authorities. Perhaps there will be little distinction between the medical responsibilities of the two. It may change the entire plan of medical practice. Such possibilities demand realistic thinking, courageous, unselfish patriotism and a high order of statesmanship. The uncertain future should make us hasten to digest the lessons of the last war, integrate civilian and medico-military agencies, and thereby be an advantage to our position in the event we are again drawn into world chaos.

In the words of Winston Churchill, "We must preserve, and if the gulf continues to widen, we must make sure that the cause of freedom is defended by all the resources of combined forethought and superior science. Here lies the best hope of averting a third world struggle, and a sure means of coming through it without being enslaved or destroyed."

To this end we should dedicate ourselves, laying aside prejudices and self-seeking and standing fast by the humanities which are the only bulwarks against ultimate disintegration of culture and civilization.

CANCER OF THE BREAST*

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WE ARE IN THE PROCESS of studying in detail the cases of carcinoma of the breast that were seen at the University of California Medical Center from July 1, 1930, to January 1, 1944. A total of 819 cases were seen in the hospital or out-patient clinic. In 83 cases no treatment was given here, but the patients have been followed. The remaining 736 patients had some form of definitive or palliative treatment. In our analysis we have used Schenck's classification.¹ It is questionable whether this is the best method of classification, but it seems to be the one in general use in the literature. In our series 173 cases, or 21 per cent, were classed as stage I. There were 201 cases in stage II and 203 in stage III. Thus, approximately half the patients were first seen when their cancer had spread to the axilla or was already far advanced. One hundred six patients (13 per cent of the series) who had had previous surgery elsewhere came to us for treatment of a recurrence (stage IV). In 53 cases roentgen ray therapy was given at our clinic following operative treatment elsewhere. Eighty-three patients who had been treated elsewhere were seen in our clinic for follow-up only. Of the entire series of 819, six patients were lost to follow up.[†]

There is such a difference of opinion in the literature today it is difficult to judge what is the best method of treatment for operable cancer of the breast. In a large general hospital handling both clinic and private patients, no definite routine can provide the specific treatment for each individual case. Our patients come from all parts of the state. Some have had a biopsy or local excision of the tumor before being referred to the clinic. It is obvious that many patients will come to us too late; nevertheless, these people still have hope and expect that we can cure them. It seems to me that we should accept every patient with cancer of the breast as one of our responsibilities. Regardless of the favorable statistics in one small selected group, we should consider what we are able to do for all patients with cancer of the breast who come to us for treatment. In our series of 819 cases, 264 patients were living and well five years or more after treatment, a survival rate of 32.2 per cent (Fig. 1). This figure does not include operative deaths or cases in which death in less than five years was due to intercurrent disease. There were four operative deaths in 470 primary surgical cases, a mortality of 0.85 per cent.

Of the group in stage I, 61.8 per cent survived five years or more regardless of the type of treatment. The five-year survival rate in stage II was 39.8 per

* Read before the American Surgical Association, St. Louis, Mo., April 20, 1949.

† This is due entirely to the diligence and hard work of our follow-up secretary, Mrs. Elinor Wells, to whom we are indebted for the completeness and accuracy of our statistics.

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cent, and in stage III, which comprised the advanced cases, it was 8.3 per cent. In these three groups which include all cases of primary carcinoma, 105 patients had roentgen ray therapy alone which in most cases was palliative. Of the 470 patients in whom a definite attempt at cure was made by surgery with or without radiation, 201 lived five years without recurrence. Thus, the five-year survival in operable cases was 42.8 per cent. In stage IV, of 106 patients who had a recurrence of a carcinoma that had been operated upon elsewhere, 24 (22.6 per cent) were living and well five years or more after treatment. In stage V, the group who had surgery elsewhere followed by roentgen ray therapy at the University of California Hospital, there were 53 living and well

FIG. 1

ALL STAGES SEEN OR TREATED 7-1-30 TO 1-1-49				
Number	L and W, 5+ Yrs	Lost to Follow-up	Percent Lost	Mortality
819	32.2%	6	.78%	4 Cases .85%

STAGE I- AXILLA NEGATIVE 173 CASES		
Treatment	No	L and W, 5+ Yrs
Radical Surg Alone	101	70.3%
Rad Surg + Preop X-Ray Therapy	22	54.5%
Rad Surg + Post op X-Ray	22	68.1%

FIG. 2

FIG. 2.—The other 28 cases are the patients either treated by simple mastectomy, roentgen ray, or lost to follow-up.

over five years, or 39 per cent. In stage VI, of 83 patients who were followed in our clinic after treatment elsewhere, 15 (18 per cent) lived five years without recurrence.

One of the puzzles of the problem of cancer of the breast is why we fail to obtain a 100 per cent cure in patients with a localized lesion without evidence either clinically or pathologically of axillary spread. It must mean that there is already extension of cancer cells that we are unable to detect at the time of surgery, or that some cells are spread during the surgical procedure. It is also curious that some of these patients have a recurrence after many years of apparent cure. We wonder where the malignant cells have been all the time and why they wait 10, 20, or even 30 years before becoming evident. The latest recurrence in my personal experience was in a doctor's widow who, 27 years after radical mastectomy, had a recurrence in the scar. She has now lived five years since resection of the recurrent tumor. Is there such a thing as cancer immunity that in some patients holds the growth in check and then for some reason is lost, allowing the cells to grow? If we had some chemical way of determining this we might be better able to cope with the disease.

McWhirter² has aroused considerable interest as well as controversy by recommending a simple mastectomy followed by postoperative roentgen ray therapy. His idea is that if the axilla is not involved there is no need to do a radical axillary dissection, and if the tumor has spread to the axilla, removal of this natural barrier, together with the trauma inflicted on the involved tissues, may well allow dissemination of cancer cells to distant sites. He reports the five-year survival rates for all operable cases treated during a ten-year period.

FIG. 3

STAGE 2 - AXILLA POSITIVE 201 CASES		
Treatment	No.	L. and W., 5+ Yrs.
Radical Surg. Alone	90	40%
Rad Surg. + Preop. X-Ray Therapy	43	41.8%
Rad Surg. + Post op. X-Ray	37	24.3%

STAGE 3 - AXILLA POSITIVE, ADVANCED 203		
Treatment	No.	L. and W., 5+ Yrs.
Radical Surg. Alone	12	16.6%
Rad Surg. + Preop. X-Ray	15	20.0%
Rad Surg. + Post op. X-Ray	16	18.7%
X-Ray Alone	103	2.91%
Simple + Post op. X-Ray	14	21.4%

FIG. 4

FIG. 3.—The other 31 patients were treated by simple mastectomy, roentgen ray, or lost to follow-up.

FIG. 4.—The other 43 patients were treated by simple mastectomy alone or were lost to follow-up.

From 1941 to 1945, when his main method of treatment was simple mastectomy with postoperative roentgen ray therapy, he had a total of 941 cases with a five-year survival rate of 55.9 per cent. This is significantly higher than that achieved during the period 1935 to 1940 when the main method of treatment was radical mastectomy and postoperative roentgen ray therapy. During this period 569 cases were treated with a five-year survival rate of 44.0 per cent. One would like to know how many of his cases were really stage I, since with simple mastectomy there is no microscopic examination of lymph nodes, and we know from experience that our judgment of the presence or absence of cancer in the axilla on clinical examination alone is wrong 30 per cent of the time. McWhirter's views are so contrary to the teaching in this country that one would hesitate to adopt this course without further proof that it is the procedure of choice. By making a special effort to have general practitioners refer all cases of cancer to the Royal Infirmary in Edinburgh, he may be getting his cases earlier and therefore have a larger percentage in which the cancer is still localized in the breast.

We have hoped that by the use of adequate roentgen therapy either before or after operation we could increase the number of five-year survivals, particularly in stage II. Statistically, the possible benefits of roentgen ray therapy are not reflected in the five-year survival rate. In stage I (Fig. 2) the highest five-year survival was in those patients who had radical surgery alone. In stage II (Fig. 3), the slightly higher survival rate with the use of preoperative roentgen ray therapy is probably not significant. Figure 4 shows that in

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stage III the use of radiation resulted in a somewhat larger percentage of five-year survivals. In this group, of 14 patients who had simple mastectomy plus postoperative roentgen ray therapy, 21.4 per cent were living and well five years later, as compared with 16.6 per cent of patients who had radical surgery alone. If a greater number of cases were represented, this might point more toward confirmation of McWhirter's ideas. Figure 5 shows the results in these three stages combined. It is seen that in the entire group the use of preoperative or postoperative roentgen ray therapy does not increase the number of five-year survivals. In another five years, with a larger series of cases, the roentgen ray therapy may show up to better advantage.

COMBINING THE THREE STAGES 557 CASES		
Treatment	No.	L. and W., 5+ Yrs.
Radical Surg. Alone	203	53.6%
Rad Surg + Preop X-Ray	80	41.2%
Rad Surg + Post op X-Ray	75	36.0%
X-Ray Alone	105	2.8%

FIG. 5

TEN YEAR SURVIVAL REGARDLESS OF TREATMENT 7-1-30 TO 1-1-49		
Stage	Number	Percent
1	37	56.9
2	27	28.4
3	0	0
1 and 2	64	41.6

FIG. 6

FIG. 5.—The other 94 patients were treated by simple mastectomy either with or without roentgen ray or lost to follow-up.

FIG. 6.—These figures and percentages are figured for the total group of 1177 cases from July 1, 1930 to January 1, 1949.

The ten-year survival rate for stage I and stage II for the period July, 1930, to January, 1939, is shown in Figure 6.

We were interested in determining whether the incidence of swelling of the arm after radical mastectomy was increased with the use of roentgen ray therapy. In our series there was no significant difference. Marked swelling occurred in 11 (3.4 per cent) of the surgically treated cases, and in 13 (5.8 per cent) cases in which surgery was supplemented by radiation therapy. In none of these patients was the swelling incapacitating.

SUMMARY

From our study so far, roentgen ray therapy as an adjunct to the surgical treatment of carcinoma of the breast has not significantly increased the five year survival rate. The study will be continued.

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DISCUSSION.—DR. WILLIAM CRAWFORD WHITE, New York City: I am a little hesitant about coming up to speak because, like Doctor Bell, I feel that I know less about this disease than I did after my first paper in 1921.

However, I have been interested recently in a study of some of the factors that perhaps are important in the surgical approach. I think it is generally agreed that we should follow out the Halsted principle, to the effect that we should remove the breast, the pectoral muscles, and the axillary contents; but there is no agreement, as far as I can discover, as to the amount of skin to be removed, the necessity of skin grafts, and the methods of undercutting the skin in a peripheral dissection.

I do not need to go into details, but all of you here know of the various arguments that are presented on this point. There are some surgeons who are convinced that one must undercut the skin well out, leaving no fat attached to the cutis, and that therefore their results will be better.

I thought that an answer to the problem would be given by a study of local recurrence. It seems to me that a report on the percentage of local skin recurrences in five years, in cases in which the disease is confined to the breast, would be a good measure for comparison. We also recognize that the accuracy of the diagnosis of localized cancer is dependent on the enthusiasm, zeal, and intelligence of the pathologist. Under such a man, the number of Group I cases will be smaller, and the local recurrences less.

A review of the reported five year local recurrence rates in various clinics, in cases of localized breast cancer, fails to prove the contention of proponents of extreme undercutting with skin grafting that their method is superior.

I think a very good point was made by Oliver and Sugerbaker, who said, "decreasing the incidence of skin recurrence would appear to be dependent among good surgeons not on the commonly discussed variations in surgical technique, but on the earlier diagnosis and surgical treatment, and on the adherence to leaving a narrower criteria of operability."

We have been convinced from some work that we did at the Roosevelt Hospital in New York that there is another factor. Brandes and I have demonstrated that quite frequently we have cancer cells on the gloves which are used in the operation. Saphir of Chicago has demonstrated cancer cells on the scalpels that were used. These loose cells may very well be an important factor in the incidence of local recurrence.

DR. GRANTLEY W. TAYLOR, Boston: It is very gratifying to hear Dr. Bell's paper. We realize that his results are entirely in agreement with the experience of most others who are engaged in this work. I think the differences which obtain are more apparent than real.

The selection of cases suitable for operation is of the utmost importance. Dr. Haagensen, of New York, tried to define these criteria recently. They are very much sharper; and all of us, as we do more breast surgery, I believe, are inclined to discard some of the cases which are borderline and in which we know we cannot bring about a fair result by surgery.

It is very difficult even to compare hospitals in one community and another on the basis of the total operability rate. We had the experience in Massachusetts when they opened the State Cancer Hospital for terminal care in advanced cases, that our operability at the Massachusetts General Hospital increased and improved very much. It wasn't a relaxation of our criteria of operability—it was the selection going on in the community which chose more favorable cases to send to us. We are primarily a surgical hospital, and send all the advanced cases to the Cancer Hospital. In spite of that, our operability roughly has maintained itself through the years because we have correspondingly been sharpening our criteria.

I want to emphasize what Dr. White said about the zeal of the pathologist in looking for axillary metastases. Obviously, if they select only those cases without any

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axillary involvement after a very thorough search, the results will be better than if that examination is purely perfunctory. Similarly, the inclusion of a number of cases with very minute axillary involvement in Stage 2 group will improve the results in that series.

We have plowed back and forth the problem of postoperative and preoperative x-ray radiation, and we are unable to demonstrate that it gives any advantage. We also have given thought to the problem of whether the wide skin removal, which Dr. White referred to, is necessary. We are unable to demonstrate that any advantage accrues to the very extensive procedure of the classical Halsted type.

Finally, I think one thing should be weighed very carefully, namely, the complications of postoperative radiation. I noticed with some disturbance and distress that the incidence of swollen arm is a very serious problem in some clinics. Dr. Treeves, of Memorial Hospital, incidentally referred to swollen arms as occurring in about 70 per cent of postoperative radical mastectomies. I cannot believe that is a true statement of incidence, because I don't see why it should happen unless it is because of the postoperative radiation.

The incidence of swollen arm in our clinic is less than 10 per cent. Dr. MacDonald recently reported from California that he had some 50 per cent of appreciably swollen arms in his series of breast cases, and he has recommended resection of the axillary vein with the idea of preventing this.

I am inclined to think that some of that may be due to postoperative x-ray, which helps to obliterate some of the residual lymphatic branches.

DR. OWEN H. WANGENSTEEN, Minneapolis: Mr. Chairman and Gentlemen, I am not an experienced breast surgeon, but I have been interested in the aggressive therapy of cancer. I do not believe real improvement will come from attempting to refine upon refinement, but as long as we have to deal with late cancer I believe that our only hope is for the surgeon to be more aggressive.

I have felt on occasion, and I suspect many of you have felt similarly in attacking cancerous lymph nodes extending up along the axillary vessels to the point where the vessels pass over the first rib, much like a hunting dog must feel when he is chasing a pheasant and the pheasant flies over a fence. The surgeon has the alternative, of course, of taking the fence down.

I have three slides which I would like to show and comment upon briefly.

(Slide) This is the first patient upon whom I operated, a patient with axillary metastases. As long as there is such a big discrepancy in the results of operation cases between Stage 1 and Stage 2 cases I think it is incumbent upon the surgeon not to retract but to expand the amplitude of our operation in Stage 2 cases.

This patient had large axillary metastases, but upon resecting the clavicle and removing the first rib six additional metastatic lymph nodes were found beyond the reach of the conventional axillary dissection. One involved lymph node was found in the brachial plexus, another at the site of juncture of subclavian and internal jugular vein, two along the inferior border of the innominate vein, and one in the second intercostal space. Moreover, in the conventional axillary dissection, the component cords of the brachial plexus can be separated. This dissection does not appear to cause areas of paresthesia or any untoward effects.

I submit that one of the weaknesses of the present so-called Halsted operation is our inability to get cancer out of the brachial plexus. I believe that by dividing the clavicle and putting it together again, and removing the first rib, in Stage II cases one can dissect the components of the brachial plexus just as well as one can the axillary vein, and there is no need to resect the axillary vein, because both the axillary vein and artery can be exposed over about a 15 cm. length and their fascial sheaths may be removed also. Careful stripping of the adventitia of the axillary vein and artery

as well as the brachial plexus over long lengths, I believe should come to be standard practice in the conventional radical breast operation.

For the patient with definite axillary metastases, I am proposing to divide the clavicle, removing the first rib, in order to permit extension of the operation in Stage II cases to include the following in addition to the conventional radical: (1) supra-clavicular dissection; (2) removal of the greater length of the internal mammary vessels beginning at their sites of origin; (3) dissection of the upper mediastinum, stripping the homolateral innominate vein in instances in which lymph node involvement beyond the first rib is observed.

(Slide) I have had experience so far, however, with only five cases. This slide indicates how the clavicle is put together with an intramedullary Kirschner wire. Patients with an intact clavicle have considerably less postoperative deformity. Moreover, they appear to have less difficulty in breathing in the early postoperative phase than does a patient in whom the inner portion of the clavicle has been excised.

(Slide) This slide shows a patient who was alleged to have a metastasis in the lung. A rounded hazel nut-sized nodule can be seen in the lateral film up against the sternum and fairly close to it. This patient had no extension beyond the conventional axillary lymph nodes. The pulmonary metastasis proved to be a fibroma in the lung.

I am certain that most of you are familiar with the writings of R. S. Handley, the son of Sampson Handley, and his associate, Thackray, at Middlesex Hospital, London. They have been removing (as Handley's father suggested in the late '20s) the lymph node along intercostal vessels in the second interspace. By making a short transverse extra pleural incision along the sternal margin in the second and fourth intercostal spaces, the greater length of the internal mammary vessels can be removed and the lymphatic tissue in juxtaposition to them.

It is too early to say what, if any, improvement will come from all this. Those of us who have had the opportunity of comparing the results of the abdominoperineal operation for low lying cancers of the rectum (6 cms. or less from the anus) with those in which the anastomotic operation is performed are aware that there is a difference—even in Stage I or so-called Dukes' group A cases without demonstrable lymph node involvement. There is an advantage in removing the *entire* lymphatic drainage area for a cancer because failure to demonstrate lymph node involvement is not synonymous with absence of small microscopic deposits. Our failure to cure 100 per cent of Stage I breast cancers is owing in part to the circumstance that there are now and then microscopic lymph node deposits beyond the site of lymph node removal, and in part to the occurrence of direct venous invasion. Moreover, I think the time is not far away too when we will hesitate less over the sacrifice of the other breast, for the systemic influence which occasioned the initial breast cancer probably continues to operate.

DR. ROBERT M. JANES, Toronto: I should like to express a somewhat different opinion than that to which we have listened.

It has been my privilege to conduct, along with the Department of Radiotherapy at the Toronto General Hospital for the past fifteen or sixteen years, a joint breast clinic. We have analyzed our results, and they show the variables that creep in, but we feel increasingly convinced that preoperative radiotherapy plays an important part.

We all know that the results of different surgeons vary at least 10 per cent, and I am sure the efficiency of radiotherapy varies at least as much.

I have slides of two patients, each operated upon eleven years ago that illustrate the results that have been obtained with preoperative radiotherapy followed by radical mastectomy.

(Slide) This the first slide of this patient. Notice the massive involvement of the axillary lymph nodes.

(Slide) After preoperative radiation.

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(Slide) Six years later. Radical mastectomy after the reaction to radiation had subsided enough to justify it. The patient still remains free of evidence of disease.

(Slide) This is the first slide of the second patient, eight months' history. Extensive ulcerating carcinoma of the breast, with axillary lymph node involvement.

(Slide) This shows the lesion almost healed following preoperative radiation.

(Slide) This slide was taken five or six years later. The patient is still free from clinical evidence of disease.

These slides can be duplicated many times. We have become increasingly convinced of the value of preoperative radiation and are employing it to a greater extent than in the past.

DR. H. GLENN BELL, San Francisco: I wish to thank all of the discussers for their remarks. Dr. White, in our clinic we have one young man in training in surgery who is the type of chap that is always asking embarrassing questions. Some time ago he came to me and wanted to know "What is an adequate skin margin in carcinoma of the breast? You give a carcinoma of the lip a centimeter and a half and say that is quite adequate. Why do you say to give a hand's breadth to a breast tumor?" He went around and measured a lot of people's hands, and he found that hands don't measure the same; so he is questioning what is an adequate skin margin. He didn't stop at that. He is now working in the laboratory, taking almost serial sections of carcinoma of the breast, to find out how far from the tumor one might have to go before he can say, "This is an adequate skin margin." I, too, have found that the statistics are very difficult to compare around the country.

I did not mention (though it will appear in my paper) the incidence of swollen arms in our clinic. We, too, have the feeling that postoperative x-ray therapy particularly would increase the number of swollen arms. There is not much difference. We divided them into mild, moderate and marked swelling. In the group that had postoperative radiation we have 6.5 per cent who had marked swelling, as contrasted to 3.2 per cent that had markedly swollen arms without x-ray therapy. None of these arms were swollen to the point that they incapacitated the patient. It did not hinder the patients' work.

MALIGNANT MELANOMA*

FORTY CASES TREATED BY RADICAL RESECTION

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SINCE THE FIRST RECORDED description of a pigmented nevus by Hippocrates,¹ melanomas have been a source of interest to physicians throughout the world. Dupuytren² is said to have been the first to recognize melanosis as a clinical entity, but Laenec³ first called the attention of the medical profession to it in a paper read before the Faculty of Medicine of Paris in 1806. It was he who used the term "melanotic" to depict one characteristic of the lesions—their color. In 1820 Norris⁴ of Stourbridge, England, reported the history of a patient whose course, during life and postmortem findings, was characteristic of melanosis, though he referred to the case as one of "fungoid disease." The name melanoma was first used by Carswell,⁵ who read a paper with Cullen before the Medico-chirurgical Society of Edinburgh in 1833 and cited two cases.

In 1858 in a treatise on melanotic cancer Pemberton⁶ described accurately the appearance of primary lesions in the skin, lower jaw, testicle, vagina and rectum, and secondary implants in the liver and other organs. He presented 25 cases, including one in which a groin dissection was performed, and suggested removal of the "integument involved and the fascia of the muscle under it." He also recommended treatment with caustic, by itself or in conjunction with surgery. Paget⁷ in 1865 reported 25 cases of melanoid cancer, in 18 of which the primary lesion was removed surgically. Five of the 18 survived for more than four years. He described three characteristics of the disease: (1) the color of the lesions due to pigment formation; (2) the proneness of the tumors to grow in or beneath pigmented moles; and (3) the multiplicity of secondary melanoid formations.

In 1907 Handley⁸ demonstrated the spread of melanotic cells along lymphatics and in fascial planes, and in 1908 Pringle⁹ first advocated the block dissection of tumor, lymphatics and regional glands which is recognized today as the treatment of choice.

ORIGIN OF CELLS

The mystery of the origin of nevus cells has never been completely solved. Three main theories have been held by different authors:

1. Broders and MacCarty¹⁰ have maintained that malignant melanotic tumors are due to migratory hyperplasia of the basal (germinative) layer of the skin, cells of this layer invading the subcutaneous tissues and distant organs.
2. Acton,¹¹ in studies on reptiles, concluded that in lower animals the melanoblasts form a primitive pigment sheet under the skin in close relation-

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ship to the angioblasts of the cutaneous respiratory capillaries. Whenever any surface downgrowth of the epiblast occurs it carries before it a portion of the primitive pigment vascular sheet, explaining the pigmented pia arachnoid of amphibians. Two types of cells are involved in melanotic tumors, melanoblasts, giving rise to melanosarcoma, and angioblasts (which, with melanoblasts, form benign moles) giving rise to malignant endotheliomas.

3. Spencer,¹² in studies on the tree frog, demonstrated that melanin pigmented cells are first developed around the neural tube for protection of the central nervous system, but later spread into the epidermis and deeper layers, and take part in the origin of melanotic tumors. Dawson,¹³ in 1929 presented histological evidence in favor of the epithelial origin of melanomas, supporting this theory by drawings of microscopic sections to show evolution of the melanoma cells from the deeper layers of the stratified epithelium. Horwitz¹⁴ in 1928 also supported this theory.

METHODS OF TREATMENT

Malignant melanomas arise in a great majority of instances from previously existing apparently benign pigmented or non-pigmented nevi. Driver and MacVicar¹⁵ found that 80 per cent of their cases gave a history of previously existing pigmented lesions. That trauma is an important cause of the malignant transformation of benign moles has been amply shown by the results of their study indicating that a history of injury preceded the transition of benign to malignant lesions was present in 58.3 per cent of cases. The cause of the transformation is not known. Ewing¹⁶ believed that if recurrence occurred following the excision of a mole, the lesion was malignant from the beginning. The Cohnheim¹⁷ theory supposed that pigmented moles harbor "sleepers" which on irritation become actively growing malignant cells.

Since most individuals have from 20 to hundreds of pigmented moles there has been considerable confusion on the part of the average physician concerning the treatment of such benign lesions. It is undoubtedly true, as Driver and MacVicar and Tod¹⁸ have pointed out, that inadequate or incomplete treatment of benign melanomata by physicians has resulted in the onset of malignant changes and in the development of malignant melanomata. A solution of the multiple mole problem has been suggested by various authors (Blair,¹⁹ Bloodgood,²⁰ Brown and Byars,²¹ Tod, Webster and Stevenson²²). Brown, flat moles and hairy moles seldom become malignant. Bloodgood reported the wide removal of 300 benign moles without complication or recurrence. Black lesions, especially if raised, which have appeared during life and are situated in areas of the body subjected to trauma should be removed by scalpel excision, leaving a surrounding margin of at least half an inch of normal skin and taking some subcutaneous tissue. Lesions showing evidence of growth, increase in vascularity or change in color should be removed widely, often with skin grafting. Blades²³ has stressed the importance of block excision of the chest wall in melanomas occurring on the chest. Pathological study of all lesions is imperative.



FIG. 1



FIG. 2

FIG. 1.—Malignant melanoma of the skin of the lower leg, showing local invasion. (Courtesy Dr. Walter Maddock)

FIG. 2.—Malignant melanoma of the chest wall, recurring in scar of previous excision. (Courtesy U. S. Army Institute of Pathology)

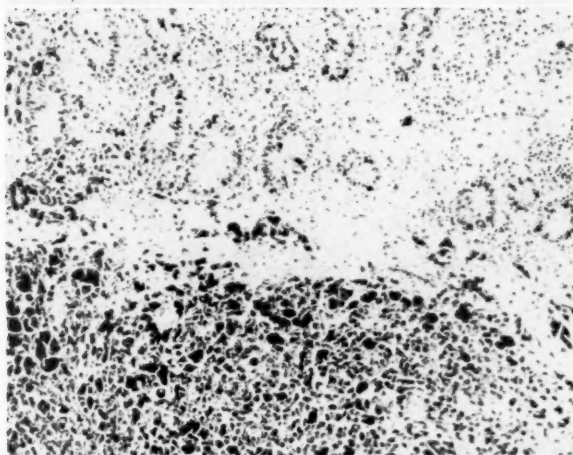
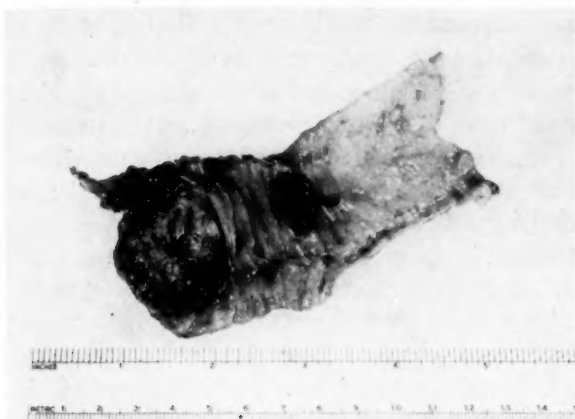


FIG. 3.—Hematogenous metastasis of malignant melanoma in the right hemisphere. (Courtesy U. S. Army Institute of Pathology)

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Once a melanoma has become malignant it may take one of three courses as outlined by Blair.¹⁹ It may grow locally, invading the surrounding skin and subcutaneous tissues (Figs. 1, 2). It may be disseminated to distant parts, carried by the blood stream to lungs, liver, brain (Fig. 3) or even intestine

A



B

FIG. 4.—Hematogenous metastasis of malignant melanoma in the intestinal wall. (Courtesy U. S. Army Institute of Pathology)

(Fig. 4). It may metastasize by way of lymphatic channels to the nearest regional nodes. Local spread of the first type can sometimes be prevented by wide excision with skin grafting. Metastasis by way of the blood stream cannot be controlled and accounts for many treatment failures. It is in lymphatic metastasis to regional nodes that, by early radical treatment our greatest hope of cure lies.

In 1907 Handley demonstrated graphically the lymphatic spread of malignant melanomas. In a patient who had died of generalized melanosis following the metastasis of a melanoma of the heel to lymph nodes in the groin he removed a strip of skin 17 cm. long from the thigh, with subcutaneous tissue and deep fascia for microscopic study. He was able to demonstrate that permeation by malignant cells takes place in a centrifugal direction from the lymphatic channels involved, extending much farther in the deep fascia than in the skin, subcutaneous tissue or muscle. In the following year Pringle described the method of nodal dissection for malignant melanoma which has not been improved upon during the past 40 years. To quote him, "a radical extirpation of the disease will most certainly be ensured by excision of the tumour with a good zone of healthy skin around it and a somewhat larger zone of the underlying subcutaneous tissue and of the deep fascia, with a broad strip of subcutaneous fascia up to and including the nearest anatomical group of glands at least, and all that is removed should be in one continuous strip as far as possible."

Occasionally, following radical dissections of this type, Pack²⁴ found that melanoma cells in lymphatic transit recurred in the wound. He has therefore recommended removal of the original lesion, followed by node dissection with removal of a strip of fascia as described by Pringle one or two weeks later if gross evidence of metastasis is present. If the nodal dissection is regarded as prophylactic, he believes it should be performed six weeks after resection of the original lesion. He reported that two thirds of the cases in which prophylactic nodal dissection was performed, without palpable nodular enlargement, showed minute foci of metastasis in the nodes removed.

DeCholnoky²⁵ has summarized the results of treatment by various authors as follows:

Summary of 5 Year Arrests						
Author	Number Cases	Location	Therapy	Cases	Time	Percent 5 Year Arrests
Adair ²⁶	70	Head, body, extrem.	Surgery	23	5 yrs.	33
Affleck ²⁷	200	Head, body, extrem.	Surgery	20	5 yrs.	11.1
Bloodgood ²⁸	200	Head, body, extrem.	Surgery	1	5 yrs.	0.1
Daland, Holmes ²⁹	82	Eye, head, body	Surgery	15	5 yrs.	18.3
deCholnoky ²⁵	26	Eye, head, extrem.	Surgery	11	5 yrs.	42.3
				5	10 yrs.	19.2
Gleave ³⁰	18	Eye	Surgery	9	5 yrs.	50
Hirtze ³⁰	54	Head, body, extrem.	Surgery	15	5 yrs.	27
			and xray	5	13 yrs.	9.2
Meland ³¹	50	Head, body, extrem.	Surgery	9	5 yrs.	18
Scharnagel ³²	70	Head, body, extrem.	Electro-surg. and xray	27	5 yrs.	39
Scott ³³	29	Head, body, extrem.	Cautery	11	5 yrs.	37.9
Average per cent of 5 year arrests.....						19.2%

Unfortunately most of these writers did not state whether or not lymph node dissections were carried out, and if so whether or not metastatic foci were found in the nodes removed.

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CLINICAL MATERIAL

Forty cases of malignant melanoma were treated by surgical extirpation and radical nodal dissection at Walter Reed General Hospital from 1942 to 1946 inclusive. In most instances the melanoma had been removed elsewhere, often at an overseas installation, the patient being transferred to this hospital because of a pathological finding of malignant growth in the lesion. Except in a few far advanced cases treatment consisted in review of the transfer slide if available, followed by radical resection of the lymph nodes draining the area involved. The nodes were resected, whether or not they were palpably enlarged. In many instances the original scar was excised and a strip of skin and fascia between it and the lymph nodes removed en bloc.

Nine of the 40 cases were regarded as far advanced, evidenced by large, fixed, palpable lymph nodes, or distant metastases. Only one of these nine cases lived for more than a few months after operation. In three of the nine, because of the degree of fixation of the involved nodes or because of distant metastases, biopsies only were performed.

TABLE I.—*Radical Resection for Malignant Melanoma*

	Total Cases		Proved Gland Metastases	Alive 1-3 yrs.	Alive 4-6 yrs.	Total Alive
	Number Cases					
Regional gland enlargement.....	25	23	92%	3	0	12%
No regional gland enlargement...	12	7	58%	9	2	88%
Gland enlargement not stated....	3	1	33%	2	0	66%
Total.....	40	31		14	2	40%

All cases were divided into two groups, depending upon the presence or absence of palpable lymph nodes. There were 25 cases in which glandular enlargement was present on admission, 12 in which it was absent and three in which records were incomplete. Among the 12 cases in which no palpable adenopathy was present at the time of the lymph node resection 7, or 58 per cent, showed pathological evidence of metastasis in the nodes removed. All of these seven patients are now alive without evidence of further metastasis or recurrence for periods varying from one to six years since operation. Of five patients without palpable adenopathy or pathological evidence of metastasis in the nodes removed one died of distant metastases four months after operation. The remaining four patients are alive and well for periods varying from one to three years since resection. Only two of 25 patients in whom nodular enlargement was present at time of operation failed to show pathological evidence of metastasis in the nodes removed. One of these patients is alive and well two years and nine months after operation, one has shown roentgenographic evidence of a metastatic lung tumor two years and six months after resection. Of the remaining 23 patients with palpable adenopathy and pathological evidence of metastasis, 20 are dead, 18 having died in less than two

years after operation. One is alive with metastases one year after operation, two have been alive and well for between two and three years.

The following histories are presented to illustrate the types of cases encountered in this study:

Case 1.—A 35-year-old male who had had a 1 cm. black, flat mole on the anterior aspect of his thigh all his life first noticed bleeding from it after crawling on his abdomen in army training in August, 1942. On January 21, 1943, the nevus was excised surgically. Pathological diagnosis was malignant melanoma. He was transferred to Walter Reed General Hospital on February 17, 1943. Examination on admission revealed the scar to be healed. No inguinal adenopathy was present. On February 26, 1943, a wide excision of the old scar was performed down to and including the deep fascia, and the defect covered by an immediate split thickness graft. On April 22, 1943, a block dissection of inguinal and iliac lymph nodes was performed. Pathological examination showed a nodule of metastatic melanoma in one of the inguinal glands removed. In September, 1948, this patient was well without evidence of recurrence.

TABLE II.—*Radical Resection for Malignant Melanoma: Cases with Proved Regional Gland Metastases*

	Number Cases	Alive, 1-3 yrs.	Alive, 4-6 yrs.	Total Alive
Regional gland enlargement.....	23	2	0	8%
No regional gland enlargement....	7	5	2	100%
Gland enlargement not stated....	1	0	0	0%
Total	31	7	2	29%

Case 2.—A 28-year-old male had had a small bluish colored nevus below the angle of his right mandible for as long as he could remember. In mid-April, 1945, he suddenly developed a painless lump about the size of a marble under the pigmented nevus. On May 23, 1945, the tumor was removed. It was darkly pigmented and was closely adherent to the capsule of the parotid gland, from which it was separated with difficulty. Microscopic diagnosis was malignant melanoma, metastatic to lymph node, complete excision doubtful. He was transferred to Walter Reed General Hospital. Examination revealed a 6 cm. incision in front of the lower lobe of the right ear with a non-tender blackish area the size of a bean 2 cm. anterior to its lower end. A few posterior cervical lymph nodes were palpable on the right side of the neck. On July 26, 1945, a right radical neck dissection was performed with extirpation of the right parotid gland. Pathological examination revealed metastatic melanoma in three lymph nodes removed from the neck and also in a lymph node imbedded in the parotid. A letter from the patient dated August 26, 1947, stated that he was well but that new nodes had appeared in the left supraclavicular region.

Case 3.—A 38-year-old man first noticed a small dark spot on the skin over the crease of his right 4th metacarpophalangeal joint in June, 1945. In November, 1945, it began to increase in size rapidly until it reached 2 cm. in diameter, and at the same time lost its pigment and became more or less flesh colored. The lesion was excised with cutting cautery. A pathological diagnosis of malignant melanoma was made. On admission to Walter Reed General Hospital on February 15, 1946, examination revealed no axillary gland enlargement. On March 13, 1946, a radical amputation of the left 4th finger was performed. On March 28, 1946, a radical left axillary node dissection was carried out. A pathological diagnosis of amelanotic melanoma, malignant, of the left hand, was made and metastatic melanoma in eight of 15 axillary nodes removed. He remained well thereafter until January, 1947, when a small wart-like nodule was found on the left

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side of his neck. This was removed and was reported to be malignant melanoma, possibly metastatic. On January 8, 1947, a complete radical left neck dissection was performed. Metastatic melanoma, amelanotic, was found in four of six glands removed. It was learned indirectly that this man was well in August, 1948, although no details of his condition were available.

Case 4.—A 30-year-old white male had had a black, smooth mole on the outer aspect of his left upper arm all his life. Because of gradual increase in size and vascularity it was removed on August 9, 1944. Pathological examination revealed malignant melanoma. He was immediately transferred to Walter Reed Hospital. Examination on admission showed a well healed scar and no adenopathy. On August 22, 1944, a radical left axillary dissection was performed. Early metastasis was found in one of the nodes removed. A letter received from this patient dated August 17, 1948, stated that he was well, symptom free and showed no evidence of recurrence.

Case 5.—A 26-year-old man reported on sick call because of the beginning enlargement of a pigmented mole on the left side of his neck behind the sternomastoid muscle. The mole was removed, leaving a wide border of normal skin around it. Microscopic examination was reported to show evidence of malignancy. He was transferred to Walter Reed Hospital. Examination on admission was non-contributory. No nodes were palpable in the neck. On September 15, 1947, a block dissection of the left neck nodes was performed. Melanotic metastases were found in the nodes removed. Two weeks later enlarged left axillary nodes were palpated. A block dissection of the axilla was performed. The nodes removed showed no evidence of tumor. In March, 1948, this patient was reported to be alive and well.

Case 6.—A 29-year-old white male noticed the appearance of a dark brown mole one half inch in diameter on his left chest wall during the summer of 1944. In August, 1944, the mole was removed surgically and was found to show evidence of malignancy on microscopic section. On transfer to Walter Reed General Hospital no adenopathy was detectable clinically, but on October 13, 1944, a left axillary gland dissection was performed. Examination of the tissue removed showed metastatic melanoma in one of nine nodes. A card received from this patient dated August 25, 1947, stated that he was well without evidence of recurrence.

Case 7.—A 35-year-old white man had had a dark brown mole three-fourths of an inch in diameter on the anterior aspect of his right thigh all his life. In November, 1943, it began to enlarge in size. In January, 1944, the mole was removed. Lymph nodes at this time were not enlarged. Pathological report of the lesion removed was that of malignant melanoma. In September, 1944, some enlargement of the right inguinal lymph nodes was noted. A radical resection of the right groin and iliac nodes was performed. Microscopic study of the nodes removed showed the presence of metastatic melanoma. In a letter dated August 9, 1948, he stated that there had been no evidence of recurrence of the melanoma or of any nodular enlargement.

Case 8.—A 35-year-old male had had a pigmented mole on the center of his back since his earliest recollection. In November, 1945, because of increased vascularity of the lesion, it was removed surgically and was reported to be cancerous by pathological section. No lymphadenopathy was present, but in January, 1946, a right axillary node dissection was carried out and in May, 1946, a similar resection on the left side. Metastatic melanoma was found in the left axillary nodes. A letter received from him on July 23, 1947, stated that he was well without evidence of recurrence.

SUMMARY

Forty cases of malignant melanoma have been treated by surgical excision and regional node resection. In 25 cases nodular enlargement was present at

time of operation. In 23 of these, metastases were present in the nodes removed. Only two of these 23 cases are now alive and well. In twelve cases no palpable adenopathy was present at time of operation. Nodular metastases were present in seven, or 58 per cent of the twelve cases. All seven are now alive and well for one to six years after radical block dissection of the regional glands involved.

Comparison of results in these two groups of cases demonstrated conclusively the importance of early radical resection of regional lymph nodes, whether or not they are enlarged, whenever a diagnosis of malignant melanoma is made. To wait for clinical enlargement of regional nodes before undertaking their block dissection is to ensure a high percentage of recurrences. Eighty per cent of patients in this series who had palpably enlarged nodes at time of operation are now dead or show evidence of recurrence. All of the patients without such preoperative nodular enlargement are now alive and well.

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DISCUSSION.—DR. ROBERT H. KENNEDY, New York City: Dr. McCune has brought up an important subject. I find, in New York at least, that there is still considerable feeling among the general practitioners, and unfortunately among a certain number of general surgeons, that with the diagnosis of melanoma (or the probable diagnosis) the patient is better off if left alone. We have to overcome that idea.

I concur with Dr. McCune entirely that there is much to be gained by doing what I like to call a "prophylactic" lymph node dissection, although all too commonly what one thinks is a prophylactic dissection is proved by the pathologist to show one node with a few melanotic cells, or even a number of small involved nodes which were not large enough for anyone to palpate.

There is a region where I do not believe in doing a lymph node dissection. We see quite a few cases where there is involvement of the region either about the umbilicus or the middle of the back. In these we have seen instances in which the metastases have gone to either axilla or either groin. Therefore I have felt that I had to wait until I had some evidence of metastases rather than doing four prophylactic node dissections which seemed more than I had a right to put the patient through.

One of the great problems in melanoma is the variation in malignancy. The individual life history shows more variation than in most types of cancer. For example, in 1927 a woman presented herself at the age of 49 who had had dental treatment fourteen years previously, in which her right lip was pinched, and ever since then she had had a black spot. This started to grow about two months before admission.

Examination showed a 3 cm. ulcerated area on the mucous membrane of the mouth within the cheek. There was also a black area on the upper lip, the lower lip, extending down into the sulcus between the cheek and jaw and extending up between three of the teeth.

My first thought was that there was no use in removing this, because of the rapid growth in only two months. But my attendant, the late Dr. Franz Torek, of this Association, said, "Well, death from ulceration in the mouth is a horrible thing. I would take it out."

So I planned carefully how I would close the area after making an excision of about one-third of the upper lip and one-quarter of the lower lip and carrying the complete cheek excision back beyond the anterior border of the masseter muscle. As I was ready to start my closure, Dr. Torek happened to come into the operating room and said, "That's fine; I wouldn't do anything more." It upset me considerably to leave

this area about three inches in diameter wide open into the mouth cavity when we were trying to relieve her discomfort. Over a period of about two months this closed in quite well.

The lesion showed all of the characteristics of malignant melanoma, including even that portion of the mucous membrane between the teeth and passing to the inside of the alveolar margin. The entire black area seemed to be melano-carcinoma.

The only further operation was a small flap turned to make a new angle of the mouth. Otherwise, that entire defect, which at one time was over three inches in diameter, closed. At that time we did not do a lymph node dissection because we all agreed we had been lucky and we expected the local lesion to recur.

At about two and one-half years she developed a number of nodes in the neck, and I felt that inasmuch as she had lived for this time without local recurrence we ought to do more. I started a complete right lymph node dissection, and when I reached the supraclavicular region I was tired of finding multiple perfectly black nodes, so I did not continue to the clavicle. By pathologic examination the only involved node was one in the submaxillary region, about 2 cm. in diameter; otherwise the nodes showed simply black foreign body pigment of some type.

I have seen her at intervals of one year after the first five years. She is now bringing up her grandchildren. It has been 22 years since excision of the original lesion, and almost 20 years since the lymph node metastasis was removed. It was worth while to do the work, but in spite of the highly malignant appearance of the cells in the slides this must really have been a melanoma of low grade malignancy.

DR. GRANTLEY W. TAYLOR, Boston: We are very much impressed with Dr. McCune's conscientious survey of his materials. Talking with Dr. White about it, we wish some of the cases might have been followed a little longer. That is something that the future holds.

We did a careful study of our material at the State Cancer Hospital and at the Massachusetts General, studying about 176 cases. First of all, I think Handley's conclusion that the spread by way of permeation is not invariably or usually a true state of affairs. If that were so we would never cure anybody by a discontinuous operation, that is, removal of the primary and the regional nodes as two separate procedures, leaving the intervening lymphatics.

I think the appearance of permeation arrives when the nodes are so blocked that the lymphatic flow is delayed or there is some stasis, and that permits the propagating thrombus to emerge from the primary focus of disease and spread itself.

The factors resulting in failure after a dissection are worth while analyzing. Dr. McCune touched on the act that blood-borne metastasis is common, and although not the earliest manifestation, as a rule, it is all too common later. We found, in analyzing our failures, that a large number of them were due to failure to control the primary disease. A recrudescence of malignant neoplasm at the primary focus after the dissection has been carried out, of course, vitiates that dissection. As long as there is any lymphatic drainage it must seek collateral channels, and often the dissection carried before eradication of local disease insists that collateral drainage pass by a very bizarre route, so that other areas of metastasis may appear which would not have supervened.

A very interesting recent example is that of a case of a woman with a lesion on her right ankle. The right groin dissection was carried out, and it was positive. A recrudescence occurred at the right ankle and the next metastasis appeared in the left groin. They must have crossed lymphatic channels going across the perineum and external genitalia to reach the opposite groin.

Dr. Kennedy referred to the difficulty of deciding what area to dissect when the lesion is in the midline or is somewhere near the belt level, where you can't be sure in which directions lymphatic drainage goes. At the present time we have a young

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man at the Massachusetts General Hospital who had a lesion over his fourth lumbar vertebra, with metastases to both axilla, and he has just had the second groin dissection carried out; so he has had dissection in all four areas.

In our study we found one person who, in addition, had a supraclavicular metastasis, so he had five of his possible radical dissections carried out.

The principal problem is to be sure that the primary disease is controlled, and therefore we invariably defer our regional dissection, if we can, until at least (we will say) two or three weeks have elapsed, until we have some confidence, from the examination of the pathological material in the local area, that probable local extirpation has been achieved.

It is very hard to train house officers to carry out the wideness of the dissection which you think is desirable. You can say "a wide excision," but they are inclined to treat these like more benign lesions of epidermoid carcinoma and basal cell carcinoma, and quite often there is some residual local pathology.

DR. KELLOGG SPEED, Chicago: Mr. President and members, I wish to say something about metastases, illustrating by one patient, and also something about the melanotic features of these tumors.

I had consult me, a few months ago, a factory superintendent 46 years of age who had bumped his knee; it had become swollen and painful. There was some enlargement, without any adenopathy in the groin or in any of the lymphatics.

(Slide) This film showed a defect in the head of the tibia, with excavation and lytic absorption, which we felt was probably a secondary tumor. He was very carefully examined by several consultants, including an ophthalmologist, and we could not find any trace or origin of the nature of the tumor. He did yield to a biopsy and a black, melanotic, soft tumor was found in the head of the tibia.

(Slide) Following discovery of this melanoma in the bone, the limb was amputated with his consent, though we knew the growth was secondary. Before that amputation he had another complete physical re-examination and all we could find were one or two small black skin tumors in the lumbar region.

I call your attention to this point at the end of the femur where the amputation was performed. There is black tissue, although the main tumor is in the tibia, as you can see. When the leg was amputated there wasn't the slightest sign of discoloration around the area of the femur, and it was perfectly clean-looking normal bone.

(Slide) This microscopic section shows the invasion of the tibial head by the typical melanotic malignant tumor.

(Slide) This section shows the involvement of the skin tumor, in the lumbar region, which was removed at the time of the amputation. It was not as large as my little finger nail.

(Slide) About four months later he returned with an exostosis developing at the end of the femur. This interfered with the wearing of his prosthesis, and therefore we removed it.

(Slide) Upon removing it we found that it had an extension of bony nature, but it was perfectly normal in color, that is, normal yellowish bone. There was no discoloration whatsoever.

Five or six days later, as his tumor lay in the laboratory in a receptacle, the excised mass of exostosis became darker and darker, and finally got very black. The pathologist, in the gross description of it, said it was probably a melanotic metastasis. The sections of that later on showed absolutely no cellular ingrowth of tumor into that exostosis. There had developed while lying in the laboratory simply a deposit of a melanotic pigment around the end of it.

The point I wish to make is that there is melanotic pigment in the blood which has never been examined or tested for, but it has been found in the urine, and if the urine of some of these patients is taken and exposed to light, and oxidized, there

will develop a black tinge or evidence of melanin from the blood as excreted by the urine which may be of help in determining whether a tumor is metastasizing and whether it is malignant. All patients with melanotic tumors, of whatever size or situation, should therefore be studied for the presence or absence of melanin in the blood serum or urine with hope of determining the prognosis in each case where the findings are positive. This test may give the first evidence of metastases in the making or already present.

DR. RALPH F. BOWERS, Memphis, Tenn.: We were stimulated at Walter Reed by Dr. McCune's work regarding two things, that melanoma is not the dangerous tumor that we all believe it to be, and that it does not necessarily deserve the existing defeatism, when compared to other dangerous malignant conditions.

I also became convinced at Kennedy Hospital, where we have had 34 of these lesions in less than three years, that there is question whether or not surgery, as we employ it today, is actually effective in the disease and whether or not the reported longevity is due to the surgery or the natural course of the tumor.

For instance, we have one patient who lived seven years without any treatment. We have had two cases with inadequate dissection or removal of melanoma from the shoulder region, who came to us four years later with metastases. Both of those patients survived more than five years, yet both had inadequate local excisions as manifested by the appearance of melanotic tissue in the scar shortly after the original excisions.

Along this line, Dr. Taylor brought out a few points that led us to the radical approach we are now using, and we have done it in six cases. The lymphatics are involved, and in the Handley procedure, we have shown that lymphatics, deep to the fascia of the muscle, are often involved, which certainly suggests that resection in continuity is not always an adequate operation.

We became convinced that one must not touch the local lesion except for the necessary biopsy, and must not manipulate or cut across lymphatic channels or its first main nodal barrier, and therefore we devised a more radical procedure in the treatment of melanoma, particularly in those cases below the umbilicus, which all of us know to be prompt killers.

We have done six cases, two of the arm and four of the leg: quarterectomy—by that I mean intrascapulothoracic amputation for the arm cases and hemipelvectomy for the leg cases. The hemipelvectomy that we employ is a little different from that described by Morton. The anterior skin incision is made in a semicircular fashion, approximately three inches above the inguinal ligament, in order that we will in no way interrupt the lymphatic channels or cut into the femoral, inguinal, or iliac glands below the level of the hypogastric artery.

Our premise states that to offer anything surgical to melanoma, we must eradicate the primary lesion, the lymphatic channels, and the main nodal barrier in one sweep, preferably without touching any of these structures during the procedure.

Our cases have not gone for a long period of time postoperatively. Frankly, we did not relish the idea of performing quarterectomy without obvious lymphatic nodal involvement. But we performed two lower quarterectomies when we could not clinically discern the lymphatic involvement. Both of those cases had involvement of a single node in the femoral group.

It is interesting to note when one incises the skin, subcutaneous tissue, and muscles above the inguinal ligament to the level of the hypogastric artery, that the iliac glands are free of disease even with demonstrable involvement in the femoral node—at least such was the situation in our leg cases. We know this is mutilating, but I think if you gentlemen were forced to view 34 cases of melanoma in a period of three years, and saw the rate of death, you would appreciate our belief that we are not too far wrong in urging these more radical procedures.

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DR. MIMS GAGE, New Orleans: That malignant melanoma should be treated, just as all carcinomas, by wide excision of the primary lesion and radical removal of the contiguous and regional lymph nodes has been ably stated by Dr. McCune. I am in complete agreement with the method he describes.

There are two points I would like to emphasize. Firstly, many surgeons and dermatologists treat potential malignant melanomas by coagulation. This method of treatment should be condemned because of the poor results, as shown by Amadon in 1933; and this has also been my personal experience. Most of the hopeless lesions which I have seen have been previously treated by the cautery method, regional and extensive metastasis being present without any evidence of local activity in the scar at the site of removal of the primary lesion. However, small black areas a millimeter or so in size can be found in the scar.

The second point is the late recurrence of distant metastasis without local activity. Three patients recently came to the Ochsner Clinic with a history of having had a melanoma removed. One patient had his eye removed twenty years before coming to the Clinic; he had a metastatic nodule in the subcutaneous tissue of the abdominal wall. The second patient had a pigmented mole on his right leg above the ankle destroyed by the electric needle. There was some pigment in the scar; about 7.5 cm. distal to the scar, and 18 cm. proximal to the scar were cutaneous nodules which proved to be carcinomatous.

The third patient had a melanotic mole in the lumbar region over the spine destroyed by active cautery ten years previously. There were some small areas of black pigment in the scar but no local activity. However, there was a larger mass in the right inguinal region. This demonstrates what happens when the primary lesions are destroyed by the method of electrical or actual cauterization. This observation is general but unfortunately is never heeded, and both the doctor and the patient become inmedicable.

I think it is difficult to formulate statistical reports regarding longevity following surgical treatment of malignant melanomas because of the late metastasis—five to 25 years after the primary operation. However, I must admit that most patients have been inadequately treated from a surgical standpoint. I believe that if all patients are treated by radical excision of the primary lesion combined with lymphatic ablation, recurrences will be negligible.

Malignant melanoma will always pose a most serious problem because of its malignant peculiarities. If the lesion demonstrates carcinomatous characteristics, the lymphatics are involved first and therefore the prognosis as regards radical surgical measures is better. However, if the lesion manifests sarcomatous characteristics, it metastasizes first via the blood stream and secondarily via the lymphatics. Therefore, there is widespread interval metastasis, which prevents radical excision of the lesion. It is in this latter group that the mortality is high and treatment is almost completely hopeless.

DR. WILLIAM S. McCUNE, Washington, D. C.: I wish to thank those who have discussed this paper and added so many helpful comments.

In regard to the variation of malignancy in the different types of melanoma, it is quite true that such variation is great and we hope in the future to be able to correlate the clinical follow-up of these patients with a review of their pathological findings.

Certainly it is true also, as Dr. Gage has remarked, that often these tumors do not recur or metastasize for as long as 12 or even 20 years, and this makes our statistics difficult to evaluate. However, we feel that since the statistics we have indicate that those patients with radical node resection fare better than those without, or than those in whom it is delayed, this procedure should be continued.

We are convinced that all involved lymph nodes should be removed by block dissection unless or until multiple distant metastases make the tumor clearly incurable. One patient with a melanoma on the anterior wall of the sternum had a bilateral

axillary gland resection, followed later by a radical neck dissection. Still later he developed an enlarged node on the opposite side of the neck, and at that point further surgical excisions were decided to be useless. He died about two years following the first operation.

Another of these patients was admitted following removal of a malignant melanoma of the hand. He had a typical Handley type of gland resection, but later developed a lesion in the skin of his neck which was diagnosed also as malignant melanoma. Whether it was a metastasis from the original lesion or another instance of the same type of tumor, we never knew. He had a radical neck dissection and he has now returned with multiple metastases.

I should like to say that in the work done at Walter Reed Dr. Bowers was a great inspiration to us. He convinced us of the wisdom of many of his radical methods of treatment.

DEVELOPMENT OF NEW METHODS FOR THE HISTOCHEMICAL DEMONSTRATION OF HYDROLYTIC INTRACELLULAR ENZYMES IN A PROGRAM OF CANCER RESEARCH*

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THE HISTOCHEMICAL ANALYSIS of the enzymatic content of normal and neoplastic tissues, as a basic approach to the cancer problem, has been the subject of considerable interest in the past decade. Further stimulus was afforded by the development of methods for the direct microscopic visualization of the sites of enzymatic activity in the tissues themselves. A number of methods for several enzyme systems have been proposed, and some of these have been used extensively.¹ In order for such methods to serve as useful tools in a variety of problems related to cancer and other medical disciplines, they must be convenient and simple to execute, they should offer clear microscopic delineation, and they should have some degree of specificity. Variation in the properties of the enzymes, such as the degree of activity or their concentration in tissues, their stability to heat and tissue fixatives, their pH optima, their solubility, and finally their hydrolytic behavior toward synthetic substrates which incorporate features for good pigment production, serve to increase the difficulties in developing means of demonstrating them.

One of the earliest methods for visualizing the sites of enzymatic activity was to utilize physiological substrates and develop pigments, where it was possible, with one of the hydrolytic products. An example of this is the method of Gomori² for alkaline phosphatase. In this case phosphoric esters of glycerol, glucose, adenosine and other substances may be used, and the phosphate produced by enzymatic hydrolysis is converted to an insoluble metal salt which may be visualized by conversion to either metallic silver or lead sulfide.

Another approach is to use a synthetic unnatural substrate, which contains a chromogenic moiety. After hydrolysis, this organic fragment of the substrate is converted to a colored pigment. An example of this is the method of Menten *et al.*³ for alkaline phosphatase. In this case a phosphoric ester of beta naphthol

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(I) is converted by enzymatic hydrolysis to beta naphthol (IV) in the presence of a diazonium salt, which immediately couples to yield an insoluble colored azo dye at the site of enzymatic activity.

The latter approach yielded a more sensitive and rapid method and appeared to offer promise of the development of methods for demonstrating enzyme systems which have hitherto been inaccessible, as well as for improving those for which methods were already in use. This approach thus formed the basis of the investigations to be presented below. Also included is a note on the outgrowth from this work of a rationale for new agents of possible chemotherapeutic value in cancer.

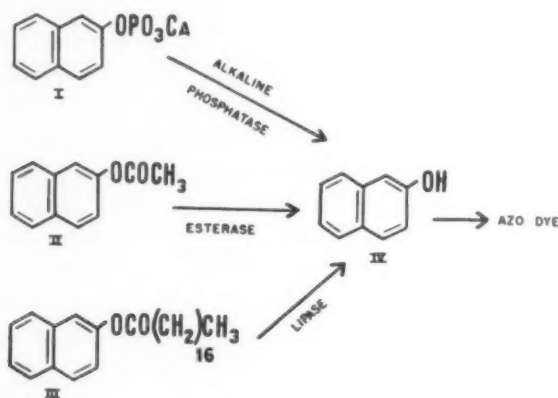


CHART I

ALKALINE PHOSPHATASE

The method of Menten *et al.*³ for alkaline phosphatase which utilized calcium beta naphthyl phosphate (I) as substrate was made practicable by the preparation of a stabilized diazonium salt of alpha naphthylamine.⁴ By this means, the method was reduced to the addition of two powders to a buffered solution into which the tissue sections were introduced for 20 minutes at 10 degrees C, by which time a satisfactory degree of staining of the section was obtained. The distribution of alkaline phosphatase in various normal tissues and tumors of humans was explored by this method.⁴ Four significant findings may be pointed out. (a) Many of the arterioles of normal tissue, particularly brain, contained alkaline phosphatase, but vessels of similar size in neoplastic tissue were nearly devoid of this enzyme. (b) Several hypernephromas were found to contain variable amounts of alkaline phosphatase. In some the concentration and pattern of distribution of the enzyme closely resembled that found in the tubular epithelium of the kidney cortex. Adrenal cortex, on the other hand, contained very little alkaline phosphatase. These findings suggest that the cell of origin of these tumors was the tubular epithelium of kidney cortex. (c) Carcinomas of stomach were practically devoid of alkaline phosphatase, whereas, carcinomas of ovary contained a delicate pattern of the

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enzyme similar to that of the ovarian stroma. This afforded a means of determining whether undifferentiated tumors of the ovary were carcinomas primary in that organ or metastatic from the gastrointestinal tract (Krukenberg).⁴ (d) Benign tumors of the human breast may or may not contain alkaline phosphatase in contrast to the regular absence of phosphatase in breast carcinoma.

ACID PHOSPHATASE

Attempts to extend the procedure for alkaline phosphatase to acid phosphatase by merely changing the pH, met with failure. Although the phosphoric acid ester of beta naphthol is hydrolyzed readily by acid phosphatase, beta naphthol (IV) does not couple well with the diazonium salt at pH 4.8, whereas

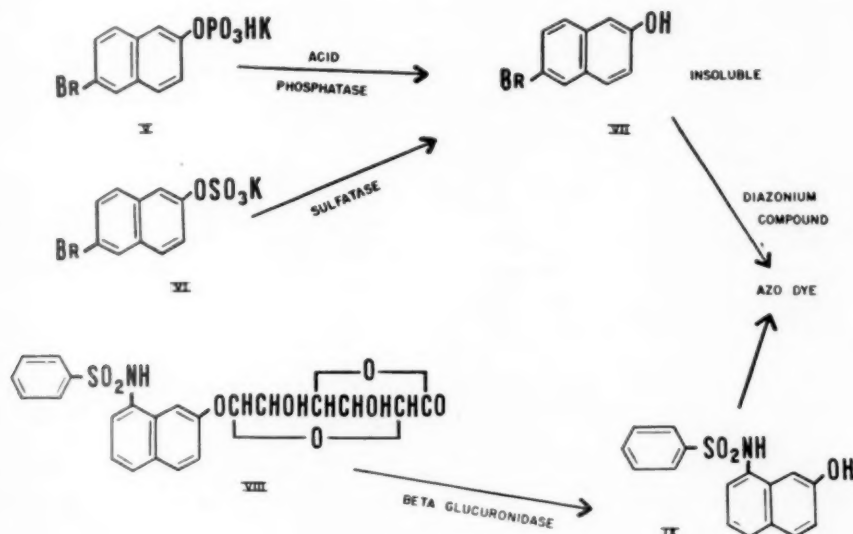


CHART II

alpha naphthol does. Acid phosphatase required longer incubation (one hour for prostate and 24 hours for other tissues) than alkaline phosphatase (20 minutes) and a higher temperature (room temperature) was required than for alkaline phosphatase (10 degrees C). Under these conditions the diazonium compound used for alkaline phosphatase decomposed extensively. Diazotized 1-amino-anthraquinone was found to be sufficiently stable under these conditions, and with calcium alpha naphthyl phosphate as a substrate, a method for acid phosphatase was provided.⁵

By using tartaric acid as an inhibitor⁵ it was possible to inhibit the cytoplasmic acid phosphatase of prostatic sections without altering the action of acid phosphatase of prostatic nuclei and of many other tissues. Evidence was thus afforded that prostatic cytoplasmic acid phosphatase and the phosphatase

of prostatic carcinoma differed from other varieties of acid phosphatase in the body.

SULFATASE AND BETA GLUCURONIDASE

The sulphuric ester of beta naphthol and the beta glucuronide of beta naphthol (isolated from the urine of rabbits fed naphthol), were readily split by the respective hydrolytic enzymes. The alpha isomers were split poorly.

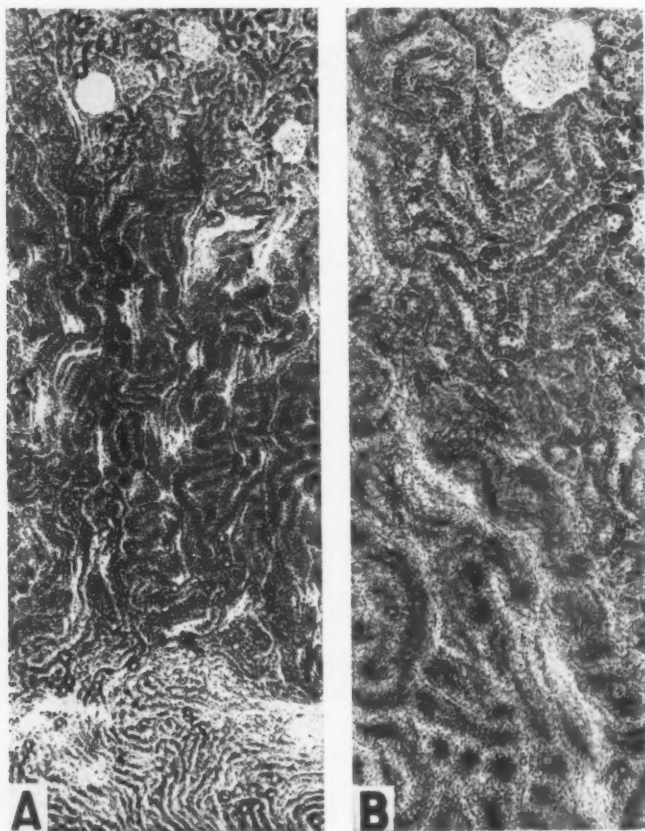


FIG. 1.—(A.) Rat kidney. Sulfatase demonstrated by a blue azo dye. Enzymatic activity is present in varying amount throughout the nephron and in the excretory ducts (not shown). Fixed in formalin for two hours, and frozen sections incubated for 24 hours. Photographed through a red filter. $\times 50$. (B.) Same section, showing two patterns of distribution of sulfatase in tubular epithelium. The convoluted tubules are diffusely stained (top), whereas, the dye is concentrated at the luminal borders in loops of Henle. Photographed through a red filter. $\times 114$.

However both enzymes have pH optima between 4.5 and 6 and, therefore, coupling with the diazonium salts did not proceed well enough for the development of good histochemical methods. The optimal temperatures were high and the time of incubation ran into many hours.

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A new principle was, therefore, evolved. Because both the sulfate and glucuronide groups conferred considerable water solubility on the substrates, it seemed possible to use colorless substrates of significantly higher molecular weight, so that after enzymatic hydrolysis the phenolic material would be sufficiently insoluble (VII and IX) to remain fixed at the site of its production, thus eliminating the need for incubation in the presence of the diazonium salts. It was important to use colorless substrates because of the danger that

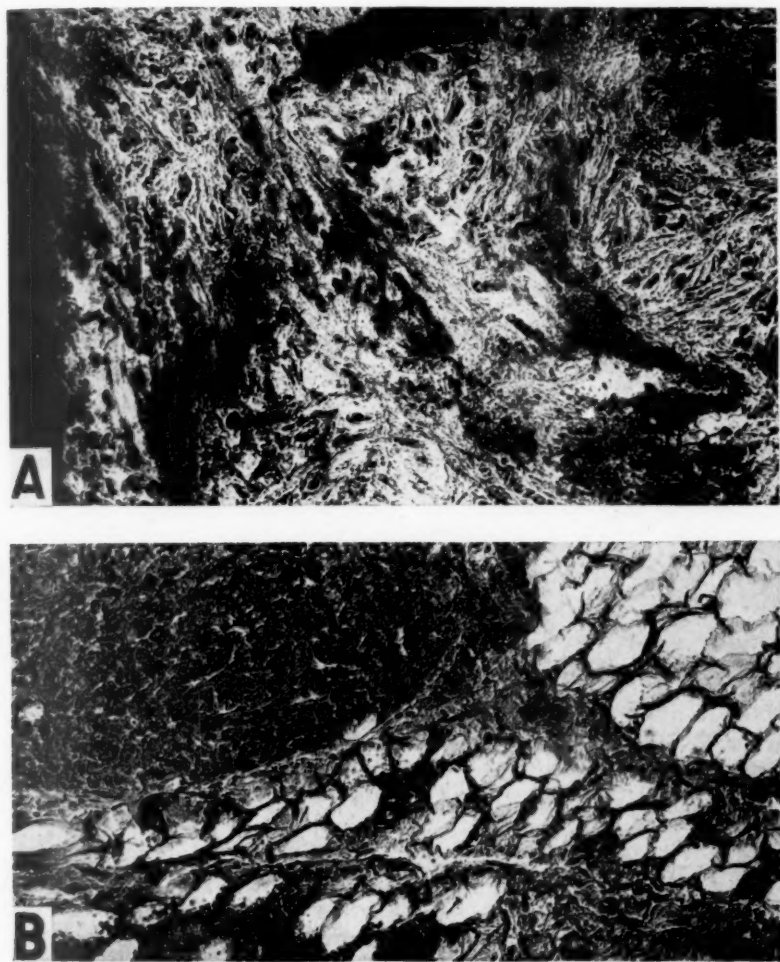


FIG. 2.—(A.) Human breast, scirrhus carcinoma. Glucuronidase demonstrated by a blue azo dye. Enzymatic activity in duct wall (left border of figure), blood vessel (top) and scattered collections of epithelial cells between the strands and whorls of fibrous tissue. Formalin fixed briefly and frozen sections incubated for 48 hours. Photographed through a green filter. $\times 165$. (B.) Human breast carcinoma. Acid phosphatase demonstrated by a blue azo dye formed after enzymatic hydrolysis of the phosphoric ester of 2-hydroxy-6-bromonaphthalene. Normal fat tissue and invading carcinoma show enzymatic activity. Fixed in acetone and embedded in paraffin. Incubated for 24 hours. Photographed through a green filter. $\times 165$.

the acid groups (sulfate and glucuronide) would result in non-specific attachment to tissue protein. After a period of incubation sufficient to insure extensive enzymatic hydrolysis, the pH could be raised to that optimum for coupling, and then with an appropriate diazonium compound (tetrazotized diorthoanisidine) a blue pigment could be produced within one to two minutes in the cold. This procedure would insure a clear background to the tissue sections. The first substrates studied (prepared from 3-phenanthrol) were not hydrolyzed rapidly enough, nor was the phenanthrol sufficiently insoluble to insure a sharp picture. Satisfactory substrates for sulfatase and acid phosphatase

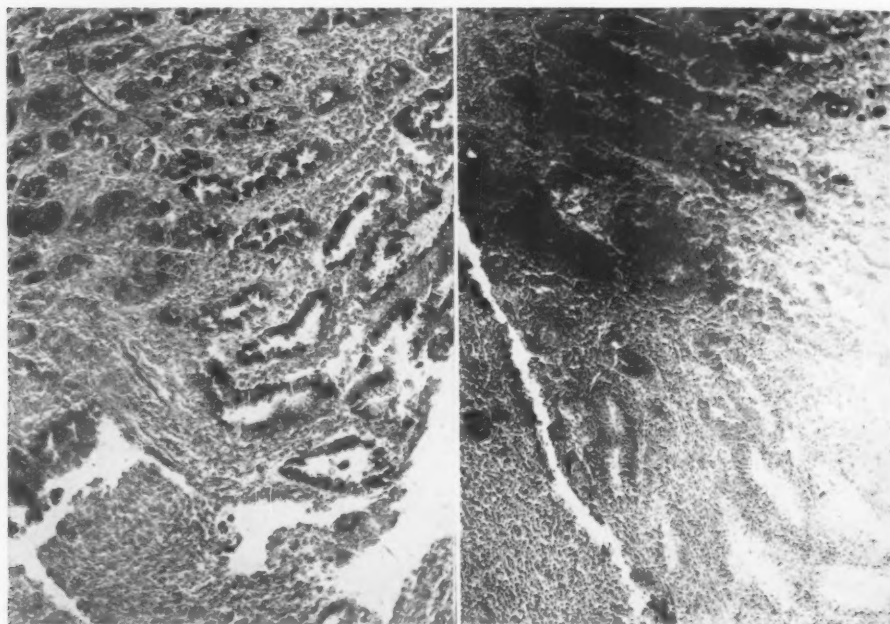


FIG. 3

FIG. 4

FIG. 3.—Human stomach; undifferentiated carcinoma. Acid phosphatase demonstrated by a blue azo dye. Acetone fixed and paraffin embedded. Incubated for 24 hours. Normal gastric mucosa (at top) and carcinoma (at bottom). All tissue contained acid phosphatase, but activity was most marked in normal glands and particularly in the parietal cells. Photographed through a green filter. $\times 112$.

FIG. 4.—Human stomach; undifferentiated carcinoma; adjacent section to that in Fig. 3. Esterase demonstrated by purplish red azo dye after 20 minutes incubation. Enzymatic activity seen only in the normal gastric glands located at the base of the mucosa. Glands near the surface epithelium were low in enzymatic activity. Parietal cells seen in upper right corner. Remnant of a gland containing esterase seen in carcinoma at lower left. The carcinoma cells were devoid of esterase. Photographed through a green filter. $\times 112$.

was provided by the appropriate esters of 2-hydroxy-6-bromo naphthalene (VII). A satisfactory substrate for glucuronidase was eventually evolved from the glucuronide of 2-hydroxy-8-benzene sulfonamino-naphthalene (IX). The glucuronide of 2-hydroxy-8-amino-naphthalene was isolated from rabbit urine after feeding 2-hydroxy-8-naphthylamine and was converted to the sub-

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strate (VIII) by treatment with benzene sulfonyl chloride. The methods for sulfatase,⁶ beta glucuronidase,⁷ as well as a new method for acid phosphatase,⁸ are now in process of being perfected. (See Figs. 1, 2 and 3.)

ESTERASE AND LIPASE

These are two distinct enzymes. In man pancreatic tissue contains both enzymes, while liver and kidney contain esterase almost exclusively. Serum normally contains esterase and no lipase (man) or traces of lipase (dog). The ideal substrates for lipase are glycerides of long chain fatty acids (C_{16} - C_{18}) and the ideal substrates for esterase are a variety of monocarboxylic acid esters of short chain fatty acids (C_2 - C_4). However, considerable overlapping occurs, and fats such as tributyrin are split by both enzymes. In an attempt to develop methods which would be specific for each, four substrates were studied. These were beta naphthyl acetate (II), beta naphthyl laurate (C_{12}) and beta naphthyl palmitate-stearate (III). The first two were hydrolyzed extensively by homogenates of liver, kidney, pancreas and by serum. The palmitate-stearate was hydrolyzed poorly by homogenates of liver and kidney or by serum, but was readily hydrolyzed by pancreatic mash. With the aid of inhibitors (arsenilate for esterase and quinine for lipase) and an activator of lipase (taurocholate) it was shown that 90 per cent of the hydrolysis of the acetate by rat liver was due to esterase, and that 80 per cent of the hydrolysis of the laurate by rat pancreas was due to lipase.⁹

The acetate proved to be a satisfactory substrate for a histochemical method for non-specific esterase.⁹ An example is illustrated in Fig. 4. By inhibiting esterase activity the same substrate demonstrated lipase activity in pancreas. Other tissues did not have enough lipase activity to be demonstrable histochemically by this method.

The palmitate-stearate (III) and laurate could not be used for a histochemical method for lipase because of their great insolubility in water and inability to diffuse into tissue sections when made into a colloidal suspension. However, the colloidal suspension served as an excellent colorimetric method for measuring *lipase activity in serum*^{10, 11} and tissue homogenates. The azo dye produced on coupling with the liberated naphthol could be extracted from the serum with ethyl acetate and measured colorimetrically. Rises in the lipase activity of serum were demonstrated in dogs after injection of mecholyl and eserine.¹⁰ This method is rapid and sensitive to minute amounts of lipase, particularly when taurocholate is used as a specific activator of lipase. Using beta naphthyl laurate, 0.002 mg. of human pancreatic tissue (homogenate), added to 0.2 cc. of serum, could be identified by its lipase activity within five hours.

ACETYLCHOLINESTERASE

In seeking a suitable substrate for acetylcholinesterase, an attempt was made to incorporate essential features of the acetylcholine structure into an aromatic phenolic compound. The acetate of 8-hydroxy quinoline methyl chloride (X) appeared to satisfy the criteria; that is, it contained a quaternary

nitrogen and two carbon atoms away from this group an acetoxy group.¹² The compound was hydrolyzed by fresh brain tissue in the cold, but unfortunately the compound hydrolyzed spontaneously, even in the cold, at pH 6.0 to a degree which mitigated against its use in a histochemical method. A more satisfactory substrate (XI), which satisfied the structural requirements, was provided by the acetate of 3-hydroxy-trimethyl-2-naphthyl ammonium iodide.¹³ Spontaneous hydrolysis was not a serious problem, and the compound was readily hydrolyzed by fresh brain tissue.

RATIONALE FOR CHEMOTHERAPEUTIC AGENTS IN CANCER

Disubstituted phosphoric esters (XII) are being prepared from the naphthols and beta chloroethyl vesicants (sulfur and nitrogen mustards). If these products are less toxic than the mustards, the selective hydrolysis of such substrates by carcinoma rich in acid phosphatase (prostatic and gastric) might liberate mustards in sufficiently high concentration to destroy tumor cells. If,

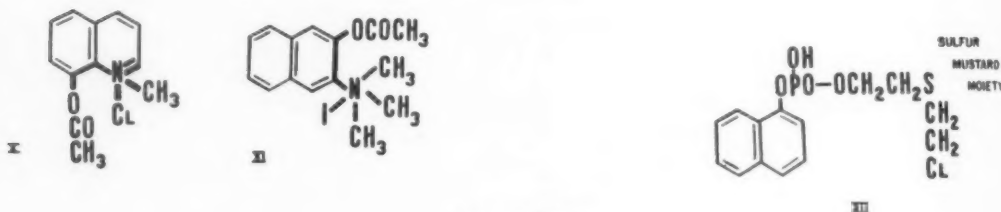


CHART III

however, the disubstituted phosphate containing a mustard moiety should prove to be more toxic than the split product, then use would be made of the fact that the beta naphthol derivative would be split by alkaline phosphatase. The widespread abundance of this enzyme in normal tissue would serve as a detoxification mechanism, and this means of detoxification would not be available to most carcinomas, which are practically devoid of alkaline phosphatase. In this way, greater specificity might be afforded mustard therapy than is possible at present. Disubstituted phosphate esters are indeed split by the phosphatases. The synthesis of the naphthyl mustard phosphate is in progress.¹⁴ Similar use could be made of the finding of Gomori,¹⁵ that phosphamidase activity is high in carcinoma. The preparation of non-toxic phosphamide derivatives of the mustards is also in progress.

Acknowledgment is due Mr. Myron Milden and Miss Marie Mollomo for technical assistance, and Mr. Leo Goodman for the photomicrography.

SUMMARY

Utilizing the principle that enzymes are able to hydrolyze synthetic substrates which may be converted to insoluble colored pigments, histochemical methods for a variety of hydrolytic enzymes have been developed and others are in process of being perfected. Principles used in developing new methods are discussed.

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DISCUSSION.—DR. ARNOLD M. SELIGMAN, Boston: In the time allotted for discussion, I might mention one outgrowth of the work reported, which should be of particular interest to you.

Utilizing the substrates which are hydrolyzed by lipase, naphthyl laurate or naphthyl stearate, it has been possible to develop a convenient colorimetric method for serum lipase. This colorimetric method is more sensitive than the present titrametric methods, which use olive oil as substrate and which depend upon titration of the fatty acid produced by enzymatic hydrolysis. Only 0.2 cc. of serum is required for the determination, and incubation can be reduced from the usual 24-hour period to four to five hours. This method should lend itself to routine use by clinical laboratories, and will serve as a useful adjunct to routine amylase determinations in the diagnosis of pancreatic disease and will be of particular value in the diagnosis of pancreatic carcinoma.

SURGICAL TREATMENT OF CONGENITAL PULMONARY STENOSIS*

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INTRODUCTION

SHUNTING BLOOD to the lungs for the relief of cyanosis due to congenital pulmonary stenosis is at present an accepted surgical procedure. Blalock and Taussig¹ opened this field of surgery by anastomosing a systemic vessel to a pulmonary artery. Potts, Smith and Gibson² described a method of making a direct anastomosis between the aorta and a pulmonary artery. Obviously, the objective of each operation is the same. Subclavian-pulmonary or aortic-pulmonary anastomoses are actually makeshift operations which do not alter the fundamental pathology in the heart but do relieve satisfactorily the distressing symptoms caused by pulmonary stenosis. Until researches on intra-cardiac surgery point the way to a means of permanently relieving pulmonary stenosis, some means of increasing the flow of blood to the lungs by circumventing the obstruction must be employed.

CHOICE OF PATIENTS FOR OPERATION

The assumption that all cyanotic children with congenital heart disease may be benefited by surgery is sadly erroneous. The incapacitated child with a typical tetralogy of Fallot who has an elevated red blood cell count, a normal or boot-shaped heart, a systolic murmur at the base of the heart, clear lung fields, and deviation of the axis to the right in the electrocardiogram, can almost always be relieved by surgery. Unfortunately, only about 60 per cent of cyanotic children with congenital heart disease fall in this typical group. The other 40 per cent have all sorts of cardiac and large vessel anomalies, many of which are not remediable by any surgical procedure known to date. Selection of patients suitable for operation from this latter group requires a profound clinical knowledge of congenital heart disease. The diagnostic work in this series of 181 patients forming the basis of this surgical report, was done by Dr. Stanley Gibson and his associates, Drs. Frank Dammann, Jakub Schlichter and Edwin Leach.

It is our policy to refuse operation to no child regardless of its condition if it can be demonstrated that cyanosis is due to diminished blood flow to the lungs. It has become apparent that the best clinical results follow surgery on patients with classical tetralogy of Fallot. Patients who have pure pulmonary stenosis or pulmonary stenosis associated with other cardiac defects such as tricuspid atresia or a single ventricle, may anticipate less satisfactory postoper-

* Read before the American Surgical Association, St. Louis, Mo., April 20, 1949.

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ative improvement. Parents are apprised of this fact before operation. It is our policy routinely to advise parents that every operation must be considered an exploratory procedure because occasionally a seemingly typical case may have abnormalities which preclude surgical relief.

The ages of these 181 patients varied from 10 weeks to 17 years. Children below one year of age are operated upon, not by choice, but only because they cannot live unless more blood is shunted to the lungs. Most of the infants below one year of age in this series were so severely hypoxic that intermittent or continuous oxygen administration was necessary.

PREOPERATIVE CARE

Regardless of the fact that diagnostic procedures have been completed in the outpatient department, cyanotic children are admitted to the hospital a minimum of 48 hours before the morning of operation. During this time observation is close for any signs of upper-respiratory infection. It is difficult in the deeply cyanotic child to evaluate a red throat or an inflamed ear drum. Rectal temperatures of 100 degrees to 100.5 degrees F. are not uncommon in the apprehensive child and if unaccompanied by any sign of cough, snuffles or contagious disease, are disregarded. Many children have had to be sent home because of the upper-respiratory infections to which they are extremely susceptible. It is, of course, contraindicated to operate on a cyanotic child with an upper-respiratory infection. At the same time it is hazardous to delay operation in the very cyanotic child because of the frequency of cerebral accidents during such infections. An infant, age six months, with a slight cold, extremely cyanotic and in desperate condition was brought in from a far western state. The danger of sending the child home seemed greater than that of intratracheal anesthesia and surgery. It died of overwhelming pneumonia five days after successful aortic-pulmonary anastomosis.

Penicillin in 100,000 unit doses twice daily is begun at least 24 hours before operation.

The apprehensive child—this includes most of them—is beneficially quieted by appropriate medication with the barbituric acid derivatives. Psychic sedation of the child, and incidentally of the parents, is routine.

Preoperative medication given one hour before operation is ordered by the anesthesiologist, Dr. William O. McQuiston. He³ advises relatively large doses of morphine and atropine for children below five years of age, including infants, and morphine and scopolamine for all patients above five years of age. For example, a three month old infant weighing eight pounds is given hypodermically morphine sulphate gr. 1/48 (1.3 mg.) and atropine sulphate gr. 1/300 (0.2 mg.). A four year old child receives morphine sulphate gr. 1/8 (8 mg.) and atropine sulphate gr. 1/200 (0.3 mg.). From five years of age until puberty, preoperative medication consists of morphine sulphate gr. 1/8 (8 mg.) and scopolamine hydrobromide gr. 1/200 (0.3 mg.). Age, not weight, determines the size of the dose. The patient should be drowsy and indifferent to surroundings when arriving in the operating room.

ANESTHESIA

In no group of patients is the skill and resourcefulness of a trained anesthesiologist more essential. The already hypoxic patient must be carried through a still more severe period of oxygen deprivation occasioned by opening the chest and occluding for a time one pulmonary artery. Doctor McQuiston has found cyclopropane the most satisfactory anesthetic agent because it allows a high concentration of oxygen and minute to minute control of the depth of anesthesia. Intubation is essential to secure an adequate airway and make possible reexpansion of the lung on a moment's notice. The operative technic is greatly facilitated if the anesthesiologist controls all respiratory movements, *i.e.*, "breathes for the patient" by rapid intermittent pressure on the anesthetic bag. Respiratory efforts during controlled respiration indicate increasing hypoxia and carbon dioxide excess and are best relieved by temporarily discontinuing the operation and reexpanding the lung if the pulmonary artery has not yet been occluded in preparation for the anastomosis. Curare is used only when it is impossible otherwise to quiet the operative field during the actual anastomosis.

Cardiac arrhythmias have not resulted from the use of cyclopropane anesthesia.

Bradycardia during operation has been benefited by intravenous administration of a very small dose of atropine, often as little as 1/1000 of a grain. Acute bradycardia or arrhythmia initiated by vagal reflexes occurring usually as dissection of the pulmonary artery is begun have been treated most satisfactorily by swabbing the hilus of the lung and the vagus nerve with a solution of 5 per cent cocaine.

TEMPERATURE CONTROL DURING OPERATION

Elevation of temperature during any prolonged operation is expected but if controlled usually occasions no anxiety. During operations on cyanotic children we have noted a more than average rise in temperature. With each degree of elevation in temperature there is approximately a 7 per cent increase in metabolism and a consequent increase in oxygen consumption. Since hypoxia is one of the chief causes of death during operation for pulmonary stenosis it follows that any means of lessening the consumption of already inadequately available oxygen is in order. For years the importance of maintaining body temperature during operation has been taught but misinterpreted. Elevation of temperature above normal during any operation is unjustifiable. McQuiston³ suggested in May of 1948 that since no means of supplying oxygen extrapulmonically has been successful, we attack the problem from the other side and try conserving oxygen by lowering the body temperature during operation in patients with severe cyanosis. About this time an infant, Thomas O., three months and 25 days old, with marked cyanosis since the age of two months, was flown to the Children's Memorial Hospital as an emergency. Attacks of unconsciousness lasting about 30 minutes were precipitated by the slightest

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exertion. Even in oxygen his condition was precarious. It was the opinion of the cardiologists, anesthesiologist and surgeon that the infant would probably die on the operating table.

The usual preparations for operation were observed. The infant received hypodermically morphine sulphate gr. 1/60 (1 mg.) and atropine sulphate gr. 1/300 (0.2 mg.) one hour before operation. (Dr. John A. Bigler, with the help of the Central Scientific Company,* Chicago, Illinois, had previously constructed an explosion-proof apparatus for the continuous recording of rectal temperatures. Later Doctor Bigler had a water mattress constructed for the control of temperatures.) Cyclopropane anesthesia was used. The infant was surrounded with ice bags. His temperature was lowered until it registered 96 degrees F. rectally, and was kept at this level for approximately 90 minutes. During much of this time no cyclopropane was necessary to maintain anesthesia. When the aortic-pulmonary anastomosis had been completed, hot water bottles were substituted and the temperature was slowly returned to normal. As soon as the temperature reached 96.7 degrees F. during closure of the chest, the infant began to react and required a small amount of cyclopropane. He was returned to his room awake and in good condition. After 24 hours he was removed from oxygen and was taking a full formula by bottle. He was discharged 14 days after operation in excellent condition.

Since then Doctor McQuiston has used controlled hypothermia during operation of 71 patients with pulmonary stenosis. No deleterious effects have been noticed. There has been no increase in postoperative respiratory complications. We believe—considering previous patients as controls—that the mortality and morbidity from severe anoxia has been lessened by the use of hypothermia.

SURGICAL TECHNIC

Aortic-pulmonary anastomosis. Although the technic of aortic-pulmonary anastomosis has been outlined in previous publications it is reviewed in detail in an attempt to answer the most commonly asked questions.

The child is laid supine on the operating table on a water mattress covered with a sheet, and anesthetized. The mattress connected with an inflow and outflow tube is partially filled with tap water. As the operation progresses, cool or even ice water is funneled into the water mattress to keep the patient's rectal temperature at about 99 degrees F. Only the very cyanotic children are cooled to 96 or 97 degrees F. It is desirable to have a continuous recording of the temperature when refrigeration is being used. After the child has been anesthetized a cannula is inserted in the right saphenous vein at the ankle for the administration of fluids, blood and medication as needed during and following operation. The child is then turned on its right side and fixed in this position with a long strip of adhesive tape across the hips and attached to the operating table to keep the child from rolling on the water mattress. The

* Construction of apparatus by M. N. States, Ph.D., and H. M. Sullivan, Ph.D.

thermocouple is inserted in the rectum and fixed with adhesive tape to prevent its being ejected. Skin preparation is with ether, iodine and alcohol.

The incision is begun anteriorly about 1 inch below and slightly lateral to the left nipple, continued straight back beneath the tip of the scapula and curved upward behind the middle of the scapula (Fig. 1A). The muscles are cut about 1 cm. below the tip of the scapula and the fourth rib is identified by palpating from the first rib downward. The chest is routinely opened through the fourth interspace except in older children or those with large chests in

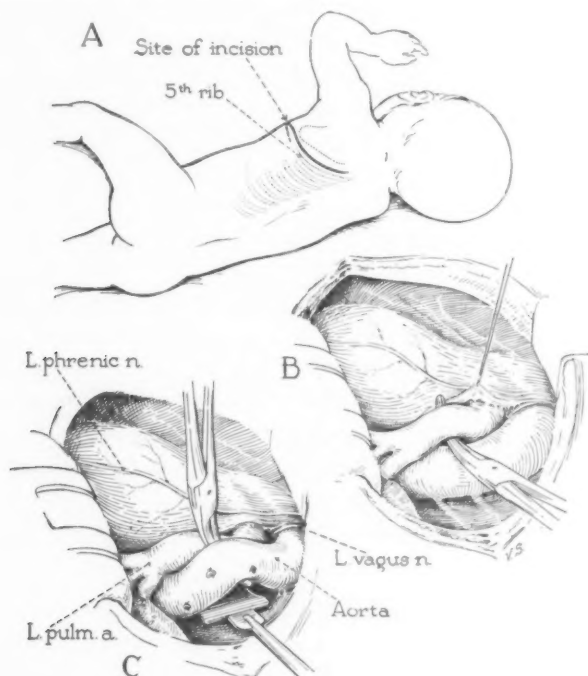


FIG. 1.—Technic of aortic-pulmonary anastomosis.

A. Lateral incision through the left fourth interspace.

B. The pulmonary artery is thoroughly freed from surrounding structures.

C. The aorta is elevated with a cystic duct forceps as the aortic clamp is slipped beneath it.

which cases the fourth rib is resected subperiosteally. The parietal pleura over the hilus of the lung is opened and the pulmonary artery identified. Exposure of this vessel will be tremendously simplified and expedited if the adventitial layer about the vessel is identified and the dissection carried through this layer.

In general the deeply cyanotic child has a smaller than average pulmonary artery buried in masses of dense connective tissue and thin-walled veins. Sponges are not used during the dissection because they are traumatic and relatively ineffective. A stream of saline solution delivered from a bulb syringe and removed by an aspirator is far more effective than sponges for

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clearing away spilled blood. The pulmonary artery, including its primary branches—usually three—is well freed from surrounding structures (Fig. 1B).

The lateral edge of the parietal pleura which was cut to free the pulmonary artery is dissected laterally to expose the aorta from its medial surface. Sometimes the vagus nerve lies anteriorly and must be freed from this layer of pleura but more often it lies deep and is not seen until later. This fold of pleura is caught with a stitch drawn laterally and held with a hemostat. As in dissection of the pulmonary artery it is well to follow the adventitial layer in freeing the aorta. However, the walls of the aorta should not be closely skinned because in so doing some of the blood supply derived from small adventitial vessels is destroyed.

Intercostal arteries vary tremendously in number and position. At the proper level opposite the pulmonary artery enough of them are doubly tied and cut to make room for application of the clamp. The average number of intercostals requiring ligation is four. Occasionally a vessel 2 to 3 mm. in diameter arising from the aorta at this level cannot be identified as an intercostal or a bronchial artery. If the vessel is directed downward, presumably towards the lung, every effort is made to avoid sacrificing it although no deleterious effects have been noted when such vessels have been ligated and cut.

At this point the lung is usually reexpanded for a few minutes even though the patient's condition seems good. The added oxygen absorbed is good insurance against the period of increased hypoxia necessitated by occluding the pulmonary artery during the anastomosis. The lung is deflated and doubly encircling ligatures of heavy silk, oiled to prevent sticking in the adventitia, are placed around the pulmonary artery and around each of its branches. These ligatures may be put on later after the aortic clamp has been applied (Fig. 2E).

The aorta, well freed, is then elevated with a cystic duct forceps and the lower half of the proper sized aortic clamp is slipped beneath the vessel (Fig. 1C). (If the clamp does not go into position easily, the reason usually is that a posterior lying intercostal artery has been overlooked.) The upper half of the clamp is adjusted. As the sections of the clamp are being brought together the adventitia of the segment of aorta which is to be isolated is grasped with a tissue forceps and drawn away from the clamp to increase the size of the occluded segment. It is essential to determine by inspection or by palpation of a thrill distal to the clamp that some blood is going through the aorta after the clamp has been tightened. How tight should the clamp be screwed? That will have to be learned from animal experimentation. It needs only to be snug. It is reassuring once or twice during the anastomosis to try the knurled nut on the end of the clamp to be sure it is not loosening spontaneously or that the assistant holding the clamp has not inadvertently loosened it. I have never had the isolated segment of aorta slip out of the clamp but it could happen with rather terrifying results.

The excess adventitia is removed with scissors from the occluded portion of the aorta where the anastomosis is to be made.

FIG. 2 (Legend on opposite page)

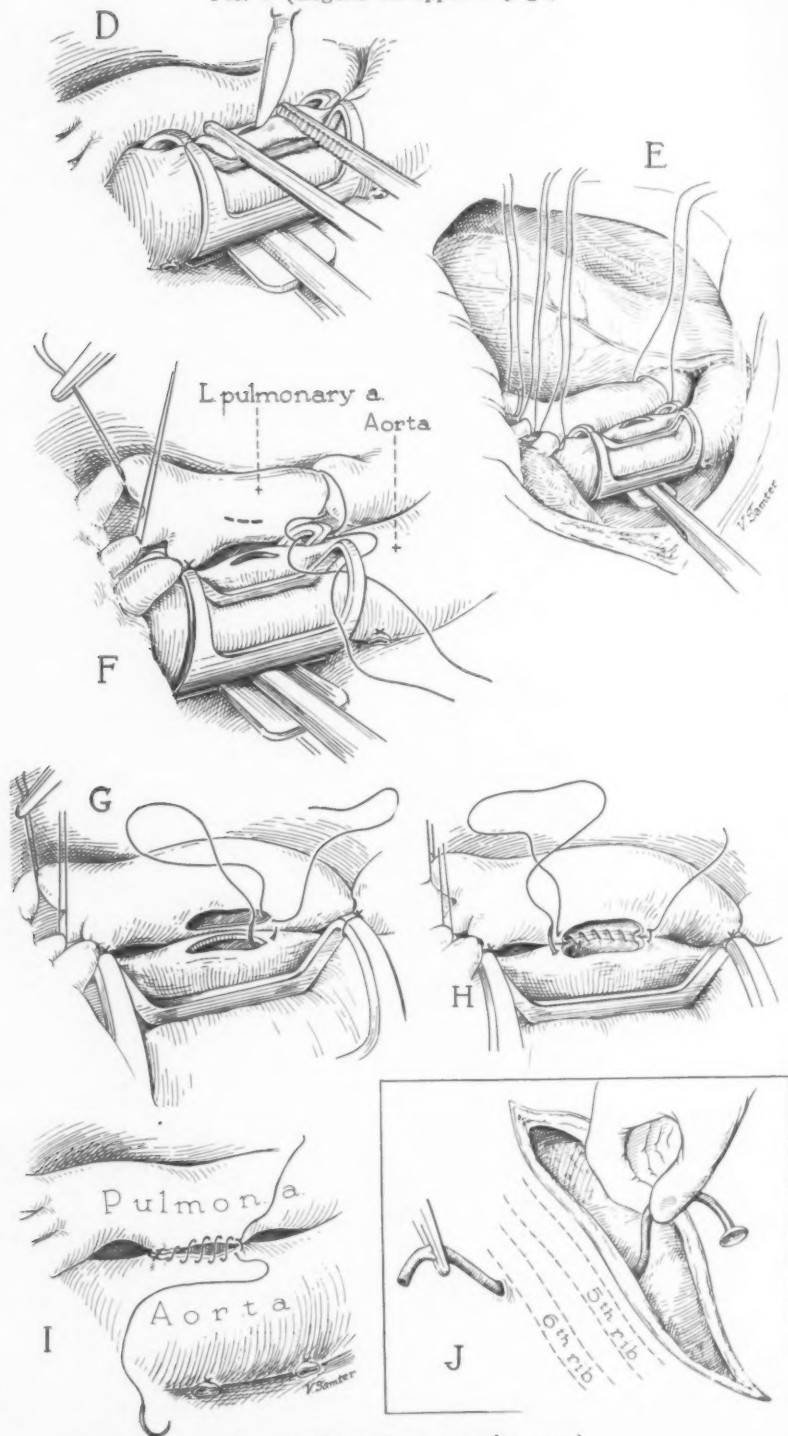


FIG. 3 (Legend on opposite page)

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The incision in the aorta must be carefully and accurately made in exactly the right place (Fig. 2D). With the open ends of a fine tissue forceps the rounded portion of the occluded segment of aorta is flattened by gentle pressure. The knife—a small blunt blade with a long handle—is directed at right angles to the flattened wall of the aorta and exactly toward the middle of the occluded portion, so that the anterior and posterior lips will be equally wide (Fig. 2D). If the incision is made off from the midline, either the anterior or posterior lip will be short and one of the rows of sutures will be put in with great difficulty. The knife is used only to make a tiny opening in the aorta. The incision is then completed to $\frac{1}{4}$ inch (6.3 mm.) with a fine pointed, angled scissors. There will be no fragmentation of the aorta in children if it is carefully cut with a scissors. (Many surgeons practicing this operation on dogs have reported difficulty occasioned by the tendency of a dog's aorta to fragment while being incised and sutured. It must not be forgotten that most laboratory dogs are full grown and many are old. Their aortas compare in age with those of a 30 to a 60 year old person. If gently handled, fragmentation of the edges of the cut aorta in a child need not be feared.)

The pulmonary artery is now tied to the aortic clamp. One end of the doubly encircling ligature about the large branch or branches of the pulmonary artery nearest the aorta is threaded through the flanges of the lower side of the aortic clamp. The other end of this ligature is drawn through in the opposite direction (Fig. 2F). These ligatures are most easily threaded on the clamp by using a large needle from which the point has been broken off for safety's sake. The pulmonary artery is then held against the aortic clamp with a cystic duct forceps while the ligature is being drawn up snugly and tied. The ligature about the pulmonary artery is tied to the upper side of the aortic clamp in a similar fashion. By tying the proximal ligature second the occluded portion of the pulmonary artery is distended with blood, making it far easier to choose the correct site for incision. The hemostat is left on the remaining medial branch of the pulmonary artery and a bit of traction kept on it after making the incision in the pulmonary artery to keep the hole open and its edges visible. The incision in the pulmonary artery is made with a knife and enlarged to proper size with a scissors to match the incision in the aorta.

FIG. 2.—Technic of aortic-pulmonary anastomosis continued.

D. Incision in the aorta must be in exactly the right place (see text).

E. Ligatures of heavy oiled silk are placed around the left pulmonary artery and its branches.

F. The lower branch of the pulmonary artery is tied to the lower edges of the clamp first, then the main vessel is tied to the upper part of the clamp.

FIG. 3.—Technic of aortic-pulmonary anastomosis continued.

G. The first stitch is so placed that the knot is outside the lumen of the vessel.

H. The posterior row of stitches, as well as the two at the lower angle, coapt the edges of the vessels adventitia to adventitia.

I. The anterior row of sutures is left loose until all the stitches have been placed. The entire anastomosis is done with one continuous suture.

J. The chest is routinely drained with a de Pezzer catheter through the sixth interspace.

The isolated segment of aorta and the occluded portion of the pulmonary artery are now washed free of all blood by a stream of saline solution. In a few instances blood has seeped into the occluded portion of the pulmonary artery. This has been due to failure to tie tightly enough one or both of the ligatures holding the pulmonary artery to the aortic clamp. The error is easily corrected by grasping the knot with a hemostat, drawing up the slack and tying a thread around the pulmonary ligature just below the knot.

The anastomosis, performed with 00000 Deknatel silk on a curved No. 9 atraumatic needle, is begun at the superior angle. The suture is carried through the pulmonary artery from the outside in and through the aorta from the inside out and tied. The knot is, therefore, outside of the lumen of the vessel (Fig. 3G). Continuing with the suture in an over-and-over manner the posterior cut edge of the pulmonary is sewed to the posterior cut edge of the aorta, adventitia to adventitia. The stitches are placed 1 mm. apart and about 1 mm. from the cut edges. It is absolutely essential that every stitch goes through all layers of the aorta. At the inferior angle the method of suture is not changed but it is necessary to carry the needle through each vessel wall separately (Fig. 3H). We do not lock the suture at the inferior angle as previously suggested but continue with this thread to bring the anterior cut edges of the vessels together intima to intima. While putting in the posterior row of stitches and those in the lower angle, the thread is drawn up gently to coapt the edges as each stitch is placed. However while placing the anterior row of sutures the thread is left loose until the last stitch has been placed. This method allows visualization and accurate placement of each stitch. Beginning then at the lower angle of the anastomosis the thread is grasped with fine tooth forceps and each stitch is drawn up with proper tension. The ends are tied and the anastomosis is complete (Fig. 3I).

The hemostat on the branch of the pulmonary artery is released first, then the lower pulmonary ligature is cut and finally the upper pulmonary ligature is cut. A small amount of bleeding may occur through the needle holes but it stops spontaneously. If the sewing has been inaccurate at any point an extra interrupted stitch may be necessary. We have never had bleeding from the posterior row of stitches. Should it occur, one would have no choice but to take down the entire anastomosis and do it over.

The aortic clamp is released *slowly*. Partial occlusion of the aorta has elevated the brachial blood pressure usually from 10 to 20 mm. of mercury, and to avoid a precipitous fall it is wise to release the clamp a bit at a time while the blood pressure is being checked. If the blood pressure drops more than approximately 20 mm. of mercury the clamp is tightened somewhat for a few minutes and again slowly released. The aortic clamp is removed. Palpation over the anastomotic channel will reveal a thrill caused by blood flowing from the aorta into the pulmonary artery. The lung is fully reexpanded by the anesthesiologist. Every chest is drained. A de Pezzer catheter with all but a flange cut away is drawn from the inside out through a tiny stab wound in the sixth

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interspace (Fig. 3J). The flange of the catheter is placed snugly against the inside of the chest.

Adjoining ribs are drawn together with two heavy catgut sutures placed subperiosteally on the inferior rib to avoid pressure on the intercostal nerve. The muscles and subcutaneous tissue are closed in layers with continuous sutures of 000 chromic catgut. The slight and questionable disadvantage of closing the chest with catgut instead of silk, I believe, is more than offset by the operating time saved in putting in continuous sutures. The operating time from skin incision to skin closure varies from one and a half to two hours.

While the anesthesiologist is making pressure on the anesthetic bag to force all air from the chest a hemostat is clamped on the drainage catheter.

The patient is turned very slowly from the lateral to the supine position. For some unknown reason the blood pressure is apt to drop alarmingly at times as the position is being changed. The intratracheal catheter is not removed until the child begins to react. Some poor risk patients who have been very hypoxic during the operation breathe very poorly for a time immediately after surgery. Such patients are kept on the operating table until they are breathing normally and their systolic blood pressure has returned to approximately 100 mm. of mercury. Occasionally a child has been kept on the table from two to three hours after the operation before it has been considered safe to move it. During this time full oxygen is given by intermittent pressure on the anesthetic bag. Respiration stimulating drugs are never used. No drug is superior to oxygen for the child who is near death from hypoxia.

SUBCLAVIAN-PULMONARY ANASTOMOSIS

Anastomosis of the proximal end of the left subclavian artery to the side of the left pulmonary artery has been accomplished successfully in 14 patients with right aortic arches. Surgical approach is the same as for aortic-pulmonary anastomosis—through the left fourth interspace or through the bed of resected fourth rib. After freeing the pulmonary artery as described above, the subclavian artery is freed from its surrounding structures to its origin from the innominate artery. The vagus nerve and its recurrent laryngeal branch looped around the subclavian artery are identified and thoroughly freed. Instead of ligating the subclavian artery at its point of branching, the individual branches, usually three, are ligated separately each with one well placed ligature. A ductus clamp, previously described,⁴ the basic principle of which is multiple tiny teeth in the apposing jaws to prevent slipping, is now placed on the subclavian artery a proper distance proximal to the point where the subclavian artery is to be cut (Fig. 4A). The subclavian artery is cut squarely across just proximal to its point of branching and is drawn out of the recurrent nerve loop and turned downward. To gain added length the subclavian artery is well freed from the carotid artery at their common point of origin. The proximal end of the pulmonary artery is now occluded with another ductus clamp or one of its modifications (Fig. 4B). The branches of the pulmonary artery are

FIG. 4 (Legend on opposite page)

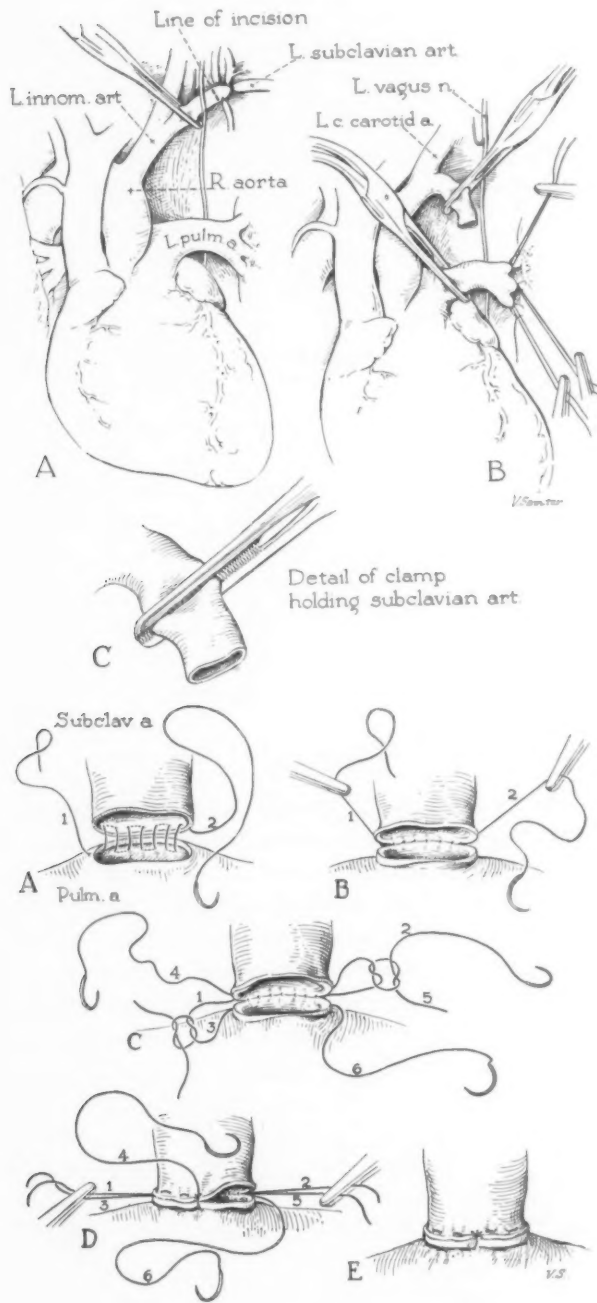


FIG. 5 (Legend on opposite page)

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occluded with doubly encircling ligatures held taut with hemostats. The technic of anastomosis is that described by Blalock (Fig. 5A-E).

Our surgical approach to the patient with pulmonary stenosis and a right aortic arch has changed (Table I). We rather stubbornly performed 22 consecutive aortic pulmonary anastomoses on the right side in patients ranging in age from four months to 16 years. In no case was it impossible to perform the anastomosis if a proper sized pulmonary was present. However, this operation is difficult on the right side because the right pulmonary artery is short and courses at a 90 degree angle to the aorta. Furthermore, the bronchus lies in the way between the pulmonary artery and the aorta. While the results eventually were satisfactory a number of children did not have an immediate typical continuous murmur and were not promptly relieved of their cyanosis following operation. Improvement was slow over a period of two to three weeks but eventually was satisfactory. One child had partial atelectasis of the lung and a bad cough, presumably due to pressure of the anastomosed vessels on the bronchus. The anastomotic channel in one child closed about four months after aortic-pulmonary anastomosis on the right side. A subclavian-pulmonary anastomosis was later done on the left side with a good result.

Our policy now is as follows: The surgical approach in all children above two years of age with pulmonary stenosis is through the *left fourth interspace*. If the arch of the aorta curves to the left an aortic-pulmonary anastomosis is done. If the arch curves to the right a subclavian-pulmonary anastomosis is done. In infants below one year of age with a right arch the subclavian artery on the left is apt to be too small for a satisfactory anastomosis and the approach is on the right side for an aortic-pulmonary anastomosis. Children between one and two years of age vary in size and the judgment (or guess work) of the operator will have to determine which side to approach. In a 15-month-old child with a right aortic arch we found a good-sized left subclavian artery and anastomosed it satisfactorily to the left pulmonary artery.

It appears that in children with left aortic arches an aortic-pulmonary anastomosis is technically simpler than a subclavian-pulmonary anastomosis on the right side; that in children with right aortic arches subclavian-pulmonary anastomosis on the left side is technically simpler than aortic-pulmonary anastomosis on the right side.

POSTOPERATIVE CARE

The anesthesiologist and the resident accompany the patient back to the room. The patient is placed in an oxygen tent rather routinely for 24 hours,

FIG. 4.—Technic of subclavian-pulmonary anastomosis.

A. The branches of the subclavian artery are tied individually; the vessel occluded with a ductus clamp and cut at the dotted line.

B. A ductus clamp or one of its modifications is applied to the left pulmonary artery. The branches are occluded with doubly encircling ligatures of heavy silk.

C. Enlarged drawing to illustrate the ductus clamp with many fine teeth in the apposing jaws which occlude, will not slip and will not injure the vessel wall.

FIG. 5.—A to E: Technic of subclavian-pulmonary anastomosis according to Blalock.

longer if necessary. A glass tube is used to connect the chest drain catheter with a tube in an under-water seal bottle. This allows easy inspection of the type of drainage from the chest. The water seal bottle is fixed to the floor with adhesive tape to prevent its being kicked over and to prevent the curious from raising the bottle. The water level in the bottle is marked by a strip of adhesive tape so that the nurse may recognize at a glance the amount of drainage from the chest. (See complications.)

TABLE I.—*Surgical Treatment of Patients with Right Aortic Arches**

Operation	Number	Deaths	Mortality
Aortic-pul. anas.....	22	2	9%
Subcl.-pul. anas.....	14	0	0
Explor. only (No pul. art.).....	5	2	40%
Totals.....	41	4	9.7%

* 22 per cent of the patients with pulmonary stenosis had right aortic arches.

A 50 cc. syringe and aspirating needle are kept at the patient's bedside. A catheter attached to an aspirating machine is used to aspirate mucus from the throat. If the rattling mucus cannot be reached the stimulus of the catheter in the throat is often effective in stimulating a productive cough. Careful

TABLE II.—*Postoperative Complications in Patients Who Recovered*

Pulmonary Complications	No. of Cases
Cough.....	22
Laryngeal edema.....	7
Laryngeal edema requiring tracheotomy.....	3
Atelectasis.....	4
Pulmonary edema.....	3
Pneumothorax.....	3*
Mild hemothorax.....	2*
Hemopneumothorax.....	1*
Effusion.....	3*
Hemorrhage.....	3
Pneumonia.....	1
Other Complications	
Cerebral anoxia	
With coma 4 days 1	2
With coma 3 days 1	
With temporary spasticity.....	3
Tonsillitis.....	2
Anuria (transfusion reaction).....	1
Wound infection severe.....	1*
Pulmonary embolus.....	1
Horner's syndrome following subclavian pul.-anas. on rt. side.....	2

* Untrained cases.

observation for obstructed respiration manifested by labored breathing and suprasternal retraction is important and calls for immediate removal to the steam room.

Penicillin units 100,000 is given intramuscularly twice a day for approximately a week following operation.

The drain is removed from the chest on the second or third day.

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POSTOPERATIVE COMPLICATIONS

As might be anticipated, by far the largest group of postoperative complications were pulmonary (Table II). Laryngeal edema occurring in ten patients was due most likely to irritation of the intratracheal anesthetic tube. Patients are watched very carefully following operation for any sign of laryngeal obstruction and promptly moved to the steam room if respiration is labored. If respiration is obstructed so that the patient fights for air, or if obstructed respiration persists and the patient becomes fatigued, a tracheotomy is promptly done. There is less danger in doing an occasionally unnecessary tracheotomy than in waiting too long to relieve the patient's struggle for air.

Should the chest be drained? is a question often asked. From our experience the answer is an unequivocal "yes." The first 13 patients operated upon for pulmonary stenosis were not drained and nine required one or more aspirations of the chest for the removal of fluid and/or air. Furthermore, these patients required repeated roentgen ray examination of the chest. The following 160 patients were drained and only seven required aspiration, because for one reason or another the drainage tube did not function efficiently. Observation of the rise and fall of the fluid in the under-water tube with each respiration reveals at a glance whether the drainage tube is functioning properly. Marking the fluid level in the drainage bottle immediately after operation makes it simple to estimate the amount of postoperative drainage. Auscultation of the chest determines whether the lung is being aerated. Postoperative roentgenological examination is practically never necessary except for study of conditions other than the accumulation of fluid or air.

Non-fatal, severe postoperative hemorrhage in the left pleural cavity occurred three times. At re-operation in one case the bleeding was found to come from the cut end of a rib which had been removed subperiosteally. The cause of bleeding in the other two was not determined. It stopped spontaneously. In all of these cases the hemorrhage was promptly detected by observation of the drainage tube and bottle. Blood was replaced by transfusion as it was being lost. Without a safety valve drainage tube the hemorrhage might not have been detected early, and the amount of blood to be replaced would have been less accurately known.

Anoxia during operation is difficult to combat and will be followed by cerebral symptoms or death depending upon the degree of deprivation. Five patients showed the effects of non-fatal cerebral anoxia following operation—two had prolonged coma and three had temporary spasticity. The only treatment employed besides the usual intravenous alimentation and careful nursing was the administration of a high concentration of oxygen. We have been singularly fortunate in that the patients who suffered from cerebral anoxia all recovered completely or died. Nothing is more tragic than the survival of a child who, following operation, is merely an unthinking metabolic machine.

Lesser complications require no discussion; minor complications which did not influence recovery unfavorably are not listed.

DISCUSSION OF DEATHS

For the causes of death in 16 patients following a successful aortic-pulmonary anastomosis see Table III. Postmortem examination was obtained on all but one. It will be noted that six deaths were due to cerebral accident. This catastrophe is very common before as well as after surgery; in fact, more children died of this complication between the time they were examined and were

TABLE III.—*Causes of Death Following Anastomosis*

Age	Number of Cases	Deaths	Time Following Operation	Causes of Death
10 wks.— 1 yr.	17	5	8 days 16 days 5 days 7 days	Pneumonia Right heart failure Cerebral anoxia Heart failure, anoxia, thrombosis of anastomosis
1-2 yrs.	22	4	5 hours 16 hours 15 hours 4 days 8 weeks	Thrombosis, cerebral sinuses Hemorrhage ruptured bronchial artery Cerebral thrombosis Cerebral hemorrhage Sepsis, infected vegetations at anasto- mosis secondary to saphenous vein infection at site of cannula insertion
2-3 yrs.	20	3	36 hours 7 days 20 days	Cerebral hemorrhage Thrombosis anastomotic site, saddle embolus. Died following embolectomy Sepsis, multiple abscesses of the left lung. Anastomosis patent
3-4 yrs.	18	0		
4-5 yrs.	18	1	5 hours	Tension pneumothorax
5-6 yrs.	14	1	During operation	Anoxia
6-7 yrs.	12	0		
7-8 yrs.	13	0		
8-9 yrs.	8	0		
9-10 yrs.	6	0		
10-11 yrs.	2	1	18 hours	Hemorrhage from intercostal artery
11-12 yrs.	9	1	30 hours	Cerebral hemorrhage
12-16 yrs.	6	0		
Totals	165	16—Mortality of 9.7%		

awaiting surgery than died of it following surgery. Basically, hypoxia is the cause of these deaths, and so long as it cannot be relieved during operation unavoidable deaths will occur.

Two children died of heart failure. Both had had decompensation relieved by digitalis before surgery. The child who has cardiac enlargement, whose liver is down, and who has previously suffered cardiac embarrassment is a very poor operative risk.

One child died the night after operation of hemorrhage from a small open intercostal artery. Either the ligature slipped off or the vessel was not tied. This child need not have died. At that time we were using plain sterile water in the drainage bottle. What blood drained into the bottle was promptly hemolyzed and did not look red enough to the nurse to sound an alarm. When the

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pulse became weak the significance of the "pink drainage" was recognized but it was too late. We now use saline in the drainage bottle, observe and mark the fluid level frequently.

One child died of tension pneumothorax before it was routine to drain the chest. At operation adhesions were separated at the apex of the lung. Upon completion of the operation the lungs were inflated and the left chest filled with saline solution. No bubbles were seen. However, a few hours after operation the child suddenly became dyspneic and died. Postmortem examination revealed the cause—tension pneumothorax from the escape of air from the apex of the lung. Since then we have drained all chests.

The case of death from a ruptured bronchial artery or a ruptured ductus arteriosus requires some explanation. At operation this child had no pulmonary artery on the left side. However, arising from the arch of the aorta just beyond the origin of the left common carotid artery was a vessel which coursed to the hilus of the left lung. The proximal 1.5 cm. of this vessel was hard and obviously occluded. Slightly above the hilus of the lung it expanded into a non-pulsating, extremely thin-walled vessel about 5 mm. in diameter. An anastomosis between this vessel, a bronchial artery or a partially obliterated ductus arteriosus, and the aorta was made. Upon release of the clamp there was a brisk thrill over the anastomotic channel. Sixteen hours after operation there was a sudden gush of blood from the drainage tube and the child died. At postmortem examination it was found that the bronchial artery or ductus arteriosus had ruptured distal to the site of anastomosis to the aorta. The anastomosis was intact, measured 4 mm. in diameter and was patent. It can only be assumed that this vessel could not withstand the strain of aortic blood pressure. It is interesting that the vessel rather than the anastomosis gave way. Further postmortem examination revealed a single pulmonary artery going to the right lung—not even a remnant of a left pulmonary artery was found. (Since this time we have performed a similar operation on an 18-month-old child with a fair result.)

The cause of death following exploration only was anoxia in six cases and anoxia and bilateral bronchopneumonia in one case. Postmortem examination was obtained in all cases. In six of these cases the pulmonary artery was merely a tiny strand of bloodless tissue and in one the pulmonary artery was present but too small for an anastomosis. In nine exploratory operations followed by survival no pulmonary artery could be found but, of course, proof of its absence is lacking.

If blood cannot be shunted to the lungs even simple exploration is apt to terminate fatally.

MORTALITY STATISTICS

Mortality statistics are always fascinating because they prove so little and can be made to prove so much (see Table IV). There were 16 deaths in 165 patients upon whom an aortic-pulmonary or subclavian-pulmonary anastomosis

was done, a mortality of 9.7 per cent. Exploratory operation alone was done on 16 patients with seven deaths or a mortality of 43.8 per cent. The overall mortality—23 deaths in 181 operations—is 12.7 per cent. There were 12 deaths in 59 children below three years of age upon whom an anastomosis was done, or a mortality of 20 per cent, while in 106 children from three to

TABLE IV.—*Mortality Statistics*

Following Anastomosis Ages	Cases	Deaths	Percentage
10 weeks-3 years.....	59	12	20
3-16 years.....	106	4	3.8
Total.....	165	16	9.7
Exploratory Operations	16	7	43.8
Grand total.....	181	23	12.7

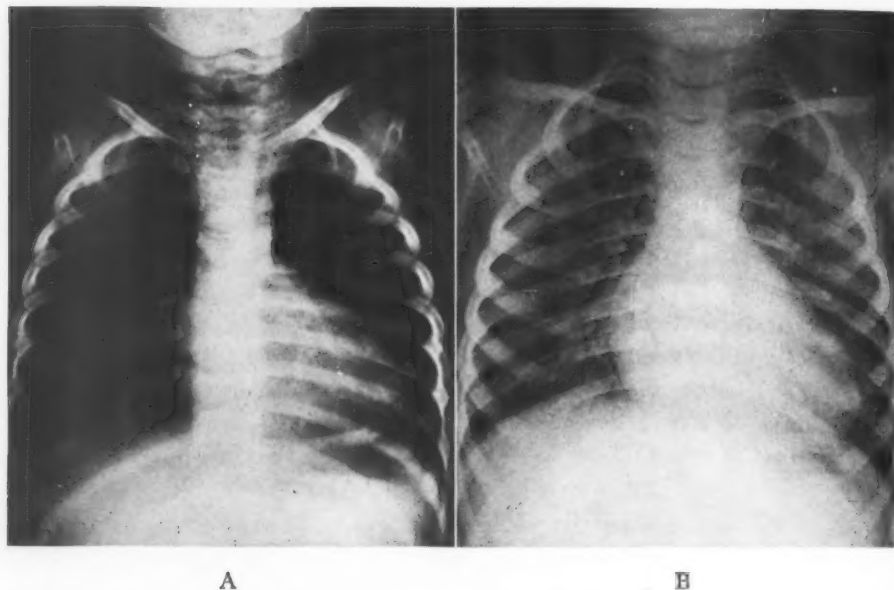


FIG. 6.—A. Preoperative roentgenogram of first patient, D. S., to have an aortic-pulmonary anastomosis, September 13, 1946.

B. Roentgenogram two years later showing about the usual postoperative enlargement of the heart and the increase in vascularity of the lung fields.

16 years of age there were only four deaths or a mortality of 3.8 per cent. In the first 10 cases below one year of age reported by Potts and Gibson⁵ there was only one death, or a mortality of 10 per cent. Four of the next seven patients died and now the mortality in children below one year of age operated upon for congenital pulmonary stenosis is 30 per cent. Statistics are interesting.

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RESULTS

The results in 135 patients who survived aortic-pulmonary anastomosis and in 14 patients who survived subclavian-pulmonary anastomosis have been satisfactory to us, spectacular to the parents, and acceptable to the children. The medical and surgical staff realize that the fundamental pathology in the heart has not been corrected and, what is more, that an added burden has been placed upon the heart by the surgical procedure. The parents see only the change in the child's color and are grateful for release from the anguish of being powerless to relieve their unhappy child. The child nonchalantly accepts his improved condition, runs and plays without thought of protecting his heart muscle.

What is the ultimate prognosis? This question is asked again and again. Too few years have passed to even guess intelligently the future of these children. Every child has some enlargement of the heart rather promptly following operation. In most instances the enlargement soon stabilizes itself—is not progressive. In Fig. 6A is shown a roentgenogram of D. S., the first patient to have an aortic-pulmonary anastomosis, operated upon September 13, 1946. Fig. 6B is a roentgenogram taken two years later. Enlargement of the heart is moderate. A few of our patients have shown excessive cardiac enlargement and two have gone into heart failure. For these I am to blame. The anastomotic channel was made too large. In the early cases we made incisions in the aorta and pulmonary artery from 5/16 to 6/16 of an inch long. *This opening was too large.* Now on young and older children alike, we routinely make the incisions in the vessels 4/16 of an inch (6.3 mm.) long, accurately measured with a caliper. This opening is large enough to relieve the major portion of the cyanosis. It is difficult in dogs to make the opening much smaller than 4/16 of an inch and have it remain patent. This undoubtedly is true for children. We still have not answered the question of whether the hole will grow with the child.

To the best of our knowledge only one anastomotic channel has closed in 149 patients who were operated upon during the past two and one-half years and survived surgery.

SUMMARY

1. One hundred and eighty-one patients with congenital pulmonary stenosis have been operated upon at the Children's Memorial Hospital.
2. No patient, regardless of condition, has been refused surgery if it could be demonstrated that there was diminished blood flow to the lungs.
3. The importance of skilled anesthesia is stressed. Cooling the patients during operation is beneficial because it lessens the consumption of oxygen.
4. The technic of aortic-pulmonary anastomosis on the left side is outlined in detail.
5. Subclavian-pulmonary anastomosis on the left is done on children above two years of age with right aortic arches.

6. Postoperative complications and deaths are outlined and discussed.
7. The overall mortality rate, 23 deaths in 181 patients, is 12.7 per cent. The mortality rate in patients upon whom anastomoses could be performed, 16 deaths in 165 patients, is 9.7 per cent.
8. The results in those patients who survived surgery have been very satisfactory.

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DISCUSSION.—DR. H. WILLIAM SCOTT, JR., Baltimore: The point that Dr. Potts made about cooling the patient certainly seems to be a good one. It is our experience at Hopkins that the majority of deaths encountered during the course of operation on cyanotic patients seem to be due to cardiac anoxia. Cooling the patient by lowering the metabolic rate and reducing the myocardial oxygen requirement should be quite helpful.

Dr. Blalock and others in our group have continued to prefer an anastomosis between the subclavian branch of the innominate artery and the side of the pulmonary. In the last 80 attempted anastomoses of this type, difficulty because of a short subclavian was encountered in only four cases. In these an end-to-end anastomosis was carried out successfully.

It should be emphasized that extensive mobilization of the systemic, as well as the pulmonary, vessels should be carried out if the subclavian branch of the innominate is going to be used.

We feel that a more accurate approximation of the intimal surfaces can be made when the subclavian is used than by using a thick walled vessel such as the aorta. Since the innominate is on the right in about 80 per cent of the cases, the incision is usually made on the right. However, in some of the larger and older patients, and in some infants, we make the incision on the left and do an anastomosis either between the subclavian branch of the aorta and the pulmonary or use the aorta itself.

When the pulmonary is very small it is our feeling that an end-to-end anastomosis is technically superior to an end-to-side anastomosis between the subclavian and pulmonary, or a side-to-side anastomosis using the aorta. With increasing experience it becomes more apparent that one should be prepared to perform the anastomosis that is best suited to the anatomical relations of the vessels encountered at operation.

DR. EGBERT H. FELL, Chicago: At the Cook County Children's and Presbyterian Hospitals in Chicago, in the past year we have performed 20 operations on 18 children. In this group of 20 operations, ten were performed on children of two years of age or less. Five of the group were between four months and one year. There were two deaths

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in this group; both of them died of thromboses. We were encouraged to attempt surgery on a still smaller or younger age group, because it has been brought out numerous times that the mortality rate is greatest in the first year of life.

We were presented with three infants very severely cyanotic, requiring constant oxygen, food parenterally, and in a semi-comatose condition. The youngest was seven and one-half weeks, weighing seven lbs.; the second was ten weeks old, weighing nine lbs.; the third five and one-half months, weighing eight lbs.

(Slide) These three cases were diagnosed by Dr. B. M. Gasul, the cardiologist and pediatrician on our service, as tricuspid atresia or non-functional right ventricle. The fundamental problem is the same as that in the tetralogy of Fallot in the fact that there is an insufficient supply of blood reaching the lung. Therefore, the problem existed of making an artificial ductus, thus shunting blood to the lung.

Life is dependent, in cases of non-functioning right ventricle, upon an interauricular septal defect and a patent ductus arteriosus, and as long as the patent ductus stays open the child exists. As the ductus closes, the severity of the condition increases. We knew that if surgery was not done these three children would not survive.

We attempted the Potts-Smith procedure, the aortic-pulmonary anastomosis in all three cases, and we were pleasantly surprised that they were all benefitted. The seven and one-half-week-old child is now over eight months old; the ten-week-old child has survived over two and one-half months, and the five and one-half-month-old child lived over six and one-half months and was brought up from southern Illinois with a severe bilateral bronchial pneumonia and died within a few hours of admission.

(Slide) This shows the right heart. You see the interauricular septal defect. There is no indication of the tricuspid valve.

(Slide) This is a very small non-functioning right ventricle. There is no communication between the left ventricle or the right auricle with the right ventricle. The pulmonary artery leads from this rudimentary structure and is small. Note the marked hypertrophy of the left ventricle.

(Slide) This is what is left of the ductus; a very small probe can be introduced into it. It is non-functioning.

(Slide) This is the left heart showing a marked hypertrophy of the left ventricle and the interauricular septal defect.

(Slide) This is the orifice of the artificial ductus as seen from the aortic side, showing that it was patent, smooth, well healed and apparently functioning well, and there was no evidence of cardiac strain or that death was due to any cardiac involvement.

We feel that these procedures should be attempted on the severely ill individuals, and that Dr. Potts and Dr. Smith have contributed a great deal to the chapter which was so well begun by Dr. Blalock.

DR. ROBERT M. JANES, Toronto: Mr. President and Members: When I read the most interesting second paragraph in the summary of this paper, it occurred to me that perhaps Dr. Potts and you would like to know something of some experimental work that has been under way in our laboratory under the direction of Dr. W. G. Bigelow for the last year and a half. The work will be presented by Dr. Bigelow in the near future, and will be published in one of the scientific journals, so I do not want to unduly steal his fire.

However, he has been good enough to loan me a few slides which show very nicely the relationship that exists between oxygen consumption and temperature.

(Slide) This slide shows graphically the relationship that exists between the oxygen consumption, as shown on the left-hand side of the graph, and cooling and rewarming, the one line being the cooling and the other the rewarming. There isn't any doubt about the fact that this oxygen consumption does fall in definite relation to the fall in temperature. The temperature you see in centigrade at the bottom.

(Slide) This is a composite graph of all dogs during the process of cooling. You will see that it follows a fairly definite pattern.

(Slide) This is a graph of the dogs again in the process of rewarming.

(Slide) One of the factors that has introduced variables in work in the past is shivering. This slide shows the increased oxygen consumption that occurs in the first place to a slight shivering, and in the second to marked shivering. It is only one of the factors that may enter into and spoil the results of these experiments, which otherwise follow a very careful pattern.

Dr. Bigelow, of course, is interested in the application of these findings to the type of surgery that Dr. Potts has been talking about; it is also applicable to studies on survival.

Dr. WILLIS J. POTTS, Chicago: Because of rather poor timing, I had to hurry over our mortality statistics. What I aimed to emphasize was that operative mortality depends upon a number of factors: choice of patients, age and coincidence, or more frankly, on runs of good or bad luck. During the terrible month of February 1948, our mortality was 50 per cent. During the past five months, there has been no mortality in a continuous series of 41 patients in the surgery of pulmonary stenosis. Operative mortality follows a surgeon like a shadow.

Assuming that no patient who has any chance of being relieved of cyanosis is refused operation, the mortality in all patients from infancy up to 16 years of age in whom a shunting operation is possible should be 10 per cent or less in a reasonably large series. In children between 3 and 16 years of age the mortality should be 5 per cent or below. In children below 3 years of age, the material is poor, the risk is great and the mortality will be high.

The most commonly asked question is this: "How large should the anastomotic channel between the aorta and the pulmonary artery be made?" A certain answer is still impossible. We now routinely make the incisions in the aorta and pulmonary artery, measured with a caliper $\frac{3}{16}$ of an inch (6.3 mm.) long. These provide a final opening after suture approximately 4 mm. in diameter. Originally we made the incisions $\frac{7}{16}$ of an inch (8 mm.) long, but since the smaller incisions give just as good results, of course, for protection of the heart muscle, we use the smaller incisions.

AN EXPERIMENTAL EVALUATION OF CERTAIN METHODS OF SUTURING THE THORACIC AORTA*

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CONSIDERABLE IMPETUS has been lent to vascular surgery in recent years through its successful application to an increasing number and variety of clinical problems. In particular, corrective procedures, as well as those designed to meliorate incapacitating congenital cardiac anomalies have both kindled anew an interest in this field. The credit for these imaginative and provocative accomplishments is shared by Gross,¹ Blalock,² Crafoord,³ and Potts.⁴ Each has indicated a personal preference for a particular type of vascular anastomosis. Most of these variants on methods of suturing blood vessels were evolved before the turn of the last century.

In 1889 Jassinowsky⁵ reported his series of successful end-to-end anastomoses of carotid arteries of sheep; his fine silk sutures were interrupted, were placed one millimeter apart and pierced only the media and adventitia. In 1896 Jaboulay and Briau⁶ reported their results on end-to-end blood vessel suture employing an everting continuous mattress stitch which permitted intima to intima approximation. Their early work on dog carotid arteries had numerous failures, but the same technic met with greater success on donkey carotid arteries; thus, early in the development of the field of vascular anastomoses the size of the vessel became recognized as an important factor determining a satisfactory end result. In 1897 Silverberg⁷ published the results of his studies. His anastomoses included all layers of the vessel. Without eversion the cut ends were united, using a continuous over and over stitch. The results were comparable to those of Jassinowsky, and Jaboulay and Briau. It is evident that the basic methods employed currently in performing vascular anastomoses were developed and tested in the experimental animal before 1900. Other technics of Murphy,⁸ Payr,⁹ and Lespinasse¹⁰ have, for the most part, been abandoned and are now mainly of historical interest. Carrel and Guthrie made several important contributions, particularly their method of triangulation, which facilitated blood vessel anastomoses.

Crafoord is reported to use a modification of methods first described by Silverberg and Jassinowsky, in which a continuous over-and-over silk stitch positioned to avoid piercing the intima, joins the vessels end to end. Gross,

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Blalock, Shumacher,¹² and others, favor the everting continuous silk mattress stitch apposing intima to intima, the suture technic identified with Jaboulay and Briaud. Crafoord believes his method affords greater tensile strength at the suture line and permits an additional few millimeters wider resection on

TABLE I.—*Materials and Methods of Suturing Used*

	6-0 Silk 27 anastomoses	5-0 Chromic 3 anastomoses	5-0 Plain 3 anastomoses
Continuous everting (mattress type) . . .			
Continuous non-everting			
1. Through all layers	30	10	3
2. Through all layers (Excess intraluminal silk)	8
3. Through media and adventitia only	4

TABLE II.—*Aortic Anastomosis Everting 6-0 Silk*

Dog No.	P. O. Day	Leaking Sacri- Pressure in mm. of Hg.	Gross Findings
35E	1	210	Thrombus extending proximally and distally from suture line. Size of thrombus 5 mm. x 5 mm. x 50 mm.
51	2	305	Thrombus 4 mm. x 5 mm. x 60 mm. extends distally and proximally.
31E	3	340	No thrombus.
29E	5	240	Very small flecks of fibrin along suture line.
44	6	275	Large thrombus 5 mm. x 4 mm. x 50 mm.
28E	6	Died of hemorrhage	Chest filled with blood clots, 2 mm. hole on back side, suture pulled through.
30E	7	Died of hemorrhage	Chest contain blood clots, suture pulled through, hole in aorta.
25E	7	460	No thrombus.
47	7	Died of hemorrhage	Suture apparently pulled through on both sides.
36	7	270	Chest wound infected. Small thrombus 2 mm. in diameter.
42	8	360	No thrombus.
24E	9	358	Small thrombus just at anastomotic line.
22E	10	Not tested	No thrombus. Dog died of prolapse of recto-sigmoid.
56E	11	360	No thrombus.
27E	11	390	No thrombus.
26E	13	370	Small amount of thrombotic deposits along suture line.
12B	14	190	No thrombus.
34E	14	760 +	No thrombus.
23E	20	520	Small thrombus, 3 mm. x 3 mm. x 5 mm.
49	20	280	No thrombus.
32E	21	352	Thrombus, 4 mm. x 5 mm. x 30 mm., attached at suture line.
21E	34	520	No thrombus.
33E	46	510	No thrombus, sutures pulling out, small pits where sutures pulled out.
52E	54	450	No thrombus, wall of vessel at anastomosis show pits where sutures have pulled through.
52	180	Not tested	No thrombus, suture pulling out, pits in intima.
52 (Reop)	180	600 +	No thrombus, sutures pulling out, pits in intima.
50	180	600 +	No thrombus, sutures pulling out leaving small pits in intima.

each side of the coarcted segment, but concedes that these benefits are associated with the development in some cases of a dissecting aneurysm. Gross and others, on the other hand, are convinced that the everting stitch minimizes the complications of both early hemorrhage and late aneurysm formation.

SUTURING THE THORACIC AORTA

Potts' use of the non-everting suture method stems somewhat from the local anatomic technical considerations posed by his clamp.

THE PROBLEM

In view of the conflicting opinions regarding the merits of the different methods of suturing the thoracic aorta after resecting areas of coarctation, this study was undertaken in an effort to shed some light on the experimental features of this problem.

Available information, and generalizations from it, on blood vessel anastomoses of the carotid artery, femoral artery and abdominal aorta appear to be inapplicable to the thoracic aorta where the combination of blood vessel size, stresses on the vessel wall, and the turbulence of blood flow through the arch

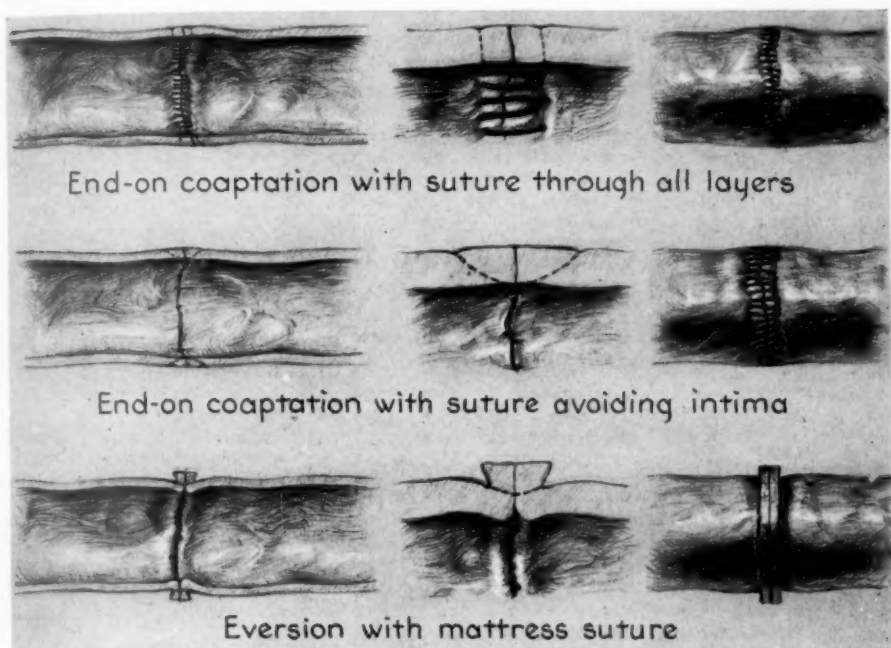


FIG. 1.—Methods of suturing the thoracic aorta.

is unique. For this reason these experiments were conducted on the thoracic aorta. The animals used were dogs and these were observed up to one year following surgery. Physiologic and pathologic studies were carried out in an attempt to evaluate the relative merits of the various technics.

EXPERIMENTAL TECHNIC

Eighty-five mongrel dogs, ranging from 5 to 15 Kg. in weight, were studied. Sodium pentobarbital was administered intravenously for general anesthesia, 30 mg. per Kg. being given initially. An intra-tracheal tube was inserted and a pneumatic cuff inflated. Respirations were maintained with

intermittent positive pressure while pure oxygen was delivered from a tank into a closed circuit. After preliminary surgical skin preparation, the left chest was entered through the fifth intercostal space. Satisfactory exposure of the upper thoracic aorta was uniformly obtained without rib resection. With the left lung partially collapsed the parietal pleura over the aorta was dissected free and preserved. No attempt was made to clear all the adventitia from the aorta as is conventionally done with smaller artery anastomoses. Care was taken to avoid damage to the thoracic duct. In about one-third of the animals the first pair of intercostal vessels was doubly ligated

TABLE III.—*End-on Coaptation with 6-0 Silk Sutures Through All Layers*

Dog No.	P.O. Day Leaking Sacri- Pressure in ficed mm. of Hg.		Gross Findings
42A	1	310	Almost complete occlusion of aorta with a clot starting at suture line. Dog paralyzed in hindquarters.
36A	3	450	No thrombus.
56A	3	400	Large thrombus 8 mm. x 20 mm. from suture line.
45	3	490	Small fibrin thrombus at suture line, 5 mm. x 2 mm. x 2 mm.
7A	3	550	Very small thrombus.
49A	4	460	Very small amount of fibrin in suture line.
4A	5	355	No thrombus.
5A	6	460	No thrombus.
2A	6	410	No thrombus.
1A	7	400	No thrombus.
37A	8	370	Small fleck of fibrin and red cells at suture line.
48A	9	345	Thrombus on posterior wall 5 mm. x 3 mm. x 20 mm.
39A	9	Not tested	Empyema, thrombus 4 mm. x 4 mm. x 15 mm. from suture line.
53	10	440	No thrombus.
55A	11	460	No thrombus.
9A	13	Hemorrhage	Hemorrhage through anastomotic line, one stitch seems to have missed catching all layers.
12A	14	310	Thrombus present 5 mm. x 5 mm. x 15 mm. from suture line.
38A	14	420	No thrombus.
6A	14	330	No thrombus.
26A	17	490	No thrombus.
8A	18	760 +	No thrombus.
13A	20	740	No thrombus.
80A	21	No leak at 600	Thrombus 4 mm. x 3 mm. x 3 mm. from suture line.
11A	55	690	No thrombus.
79A	60	600 +	No thrombus.
34	72	No leak at 740	No thrombus.
52	180	Not tested	No thrombus.
52 (Reop)	180	No leak at 760	No thrombus.
10A	365	Not tested	No thrombus.
3A	365	760 +	2 mm. x 3 mm. x 3 mm. well organized and firmly adherent to vessel.

and divided. The distal aortic arch and the proximal thoracic aorta were freed and mobilized. Specially modified intestinal clamps were applied across the aorta and the vessel divided. In some animals a segment varying from one to two centimeters in length was removed before doing the anastomosis; this was largely from the group in which intercostal vessels were divided. Suturing was usually started from the posterior portion of the vessel and was continued around anteriorly.

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Eight series of experiments were conducted. Three different types of suture materials were employed: 6-0 braided silk,* 5-0 medium chromic catgut,† and 5-0 plain catgut.‡ All materials were swaged onto three-eighths curved fine, atraumatic, Kalt needles. Three different methods of suturing were employed; these are illustrated in Figure 1. Table I indicates the number of dogs handled in the varying manners.

Series I consisted of 26 dogs‡ in which the severed ends of the aorta were joined with a continuous everting mattress stitch of 6-0 braided silk. Sutures were placed one and a half millimeters from the vessel edge and one and a half millimeters between the return loops of the mattress suture. All of these were anchored by ligation at the midpoint.

Series II consisted of 29‡ dogs in which the severed ends of the aorta were anastomosed with a continuous, non-everting, over-and-over stitch of 6-0 braided silk which passed through all layers of the aorta-intima, media and adventitia. These sutures were placed one to one and a half millimeters from the cut edge and were one millimeter apart. In most instances a single strand was employed to sew the entire vessel while in a few the suture was anchored by ligation at the midpoint.

Series III consisted of eight dogs, in which a continuous non-everting anastomosis was done, employing 6-0 braided silk. The suture material passed through all layers of the aorta, but stitches were placed approximately two and one-half millimeters from the cut edge. By such means excessive amounts of silk were deliberately exposed in the lumen. The distance between sutures was the same as in Series II.

Series IV consisted of four dogs, in which a continuous non-everting anastomosis was performed, employing 6-0 braided silk. Here the suture material passed through only the media and adventitia and the point of entrance of the suture into the vessel wall was two and one-half millimeters from the vessel's cut edge.

Series V and VI consisted of 3 and 10 dogs respectively. 5-0 medium chromic catgut was employed. Stitching was done the same as in Series I and II respectively.

Series VII and VIII consisted of three dogs each. In these experiments 5-0 plain catgut was used and again stitching was done in the same manner as in Series I and II respectively.

Following the completion of the anastomosis the clamps were removed rapidly, first the distal and then the proximal clamp. There was uniformly an acceleration of the heart rate upon the rapid removal of the clamps, but no other ill effects were noted. Bleeding from the operative suture line was infrequent regardless of the method used. In an occasional instance after removal of the clamps, blood pumped out through the suture line. Cessation

* Average tensile strength found to be 410 Gm.

† Average tensile strength found to be 560 Gm. This and the above were supplied through the courtesy of Johnson and Johnson, New Brunswick, N. J.

‡ One animal was operated upon more than once.

FIG. 2

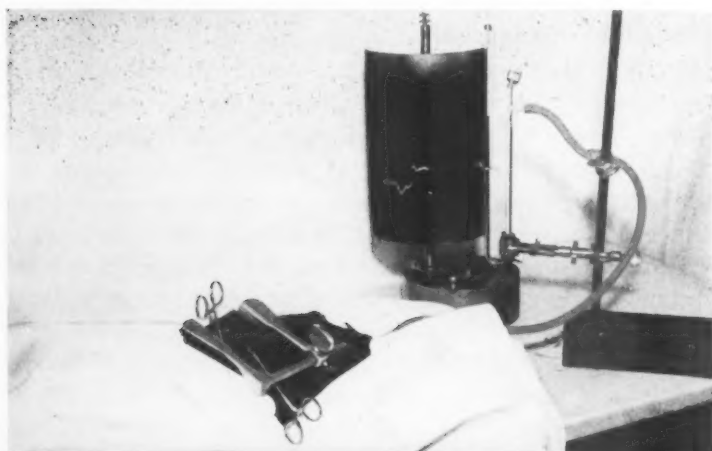


FIG. 3

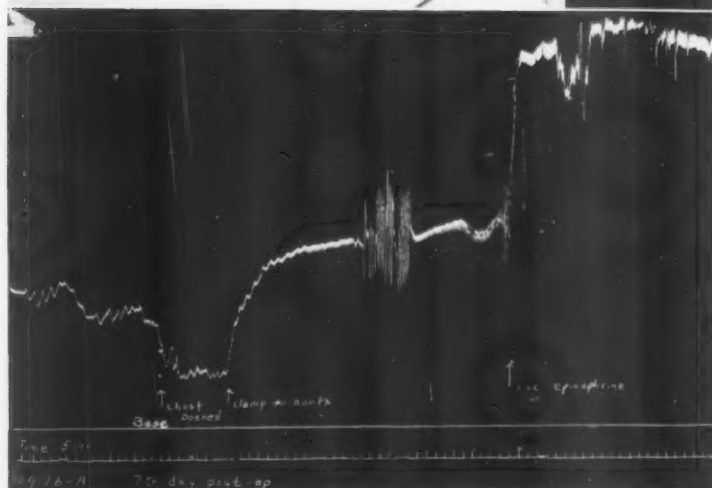


FIG. 4



FIG. 2.—Apparatus for measuring intraluminal pressure in situ.
 FIG. 3.—Reproduction of kymographic tracing. Maximal pressure of 350 mm. of Hg. was obtained.
 FIG. 4.—Apparatus for measuring maximal intraluminal pressure tolerated by the aorta.

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of this hemorrhage occurred regularly after mild pressure was patiently maintained over the bleeding point with a finger and moist gauze for three to five minutes. The anastomotic site was in all instances carefully pleuralized. Pericostal sutures were placed, the lungs fully expanded, and the chest wall muscles then closed in layers. Postoperatively the dogs recovered in their cages, soon resumed full activity, and ate regular kennel diet. In no instance were anticoagulants administered pre- or postoperatively.

Complications as a direct result of surgery included empyema, paralysis of the hind legs, and hemorrhage at the anastomosis. Early in the experiments a suppurative pleuritis occurred in about one-third of the animals. The subsequent routine instillation of 50,000 units of penicillin into the pleural space eliminated this complication. Paralysis, transient or permanent, of the lower

TABLE IV.—*End-on Coaptation with 6-0 Silk Suture Avoiding Intima*

Dog No.	P.O. Day Leaking		Gross Findings
	Sacri-ficed	Pressure in mm. of Hg.	
50A	3	270	Very small thrombi started from intimal edge 2 mm. x 3 mm. x 16 mm.
78A	6	310	No thrombus.
51A	14	450 +	Died of distemper. No thrombus.
53A	50	No leak at 450	No thrombus.

TABLE V.—*End-on Coaptation with Excess Silk in Lumen*

Dog No.	P.O. Day Leaking		Gross Findings
	Sacri-ficed	Pressure in mm. of Hg.	
45A	6 hrs	240	Cause of death indeterminate. Small fibrinous deposits around sutures.
49A	4	460	Small thrombus 2 mm. x 3 mm. along sutures
47A	6	320	Small thrombotic deposits along sutures.
48A	9	345	Large thrombus fills lumen of vessel.
43A	13	No leak at 680	Empyema. Only small thrombi around sutures.
46A	17	380	No thrombus.
44A	21	420	Small thrombus 2 mm. x 3 mm. x 3 mm.
54A	30	No leak at 450	No thrombus.

limbs, along with bladder and rectal sphincter dysfunction, occurred, especially in older dogs, when the aorta was clamped for longer than 25 minutes. With an increasing experience most anastomoses were accomplished in about 15 to 18 minutes. The animals which died on the table from immediate intra-thoracic hemorrhage have been omitted from this series; such hemorrhages were primarily the result of faulty operative technic, and occurred in the earlier phases of the problem. Delayed hemorrhages will be discussed below.

The tensile strength of the healing or healed aorta was assayed at intervals ranging from one day to one year. At the onset a number of anastomoses were tested in situ. (Figure 2.) At such times the dogs were anesthetized with sodium pentobarbital; an intra-tracheal airway was inserted; respirations were

maintained with intermittent positive pressure; the carotid artery was cannulated for recording arterial pressures with a mercury manometer; and the left chest was opened without sterile technic. The anastomotic site was observed. A basal blood pressure reading was obtained. The aorta was cross clamped distal to the anastomosis and blood pressure tracings secured. Subsequently, 1 cc. of 1 to 1000 epinephrine was injected into the left auricular appendage and repeated blood pressure tracings were recorded (Figure 3). Arterial blood pressures as high as 350 mm. of mercury were obtained in this manner and in only one instance* did bleeding from the suture line follow such an examination.

Finally the distal aortic arch and thoracic aorta were excised together, one end of the aorta was cannulated, and the other clamped (Figure 4), and with the specimen under water the sutured ends gradually distended with compressed air until the first leak was noted. This value was measured with a mercury manometer. The vessels were then opened and photographs taken. The character of the intraluminal surface of the anastomosis was noted, with special attention directed to the presence or absence of thrombi. Appropriate sections for microscopic examination were fixed in 10 per cent formalin. These were stained with hematoxylin and eosin and van Gieson's stain.

EXPERIMENTS

Tables II to IX summarize the results of 88 satisfactory protocols in the eight series of experiments. This is graphically represented in Figures 5 to 8. Detailed consideration is given below to (1) the intraluminal pressures tolerated by sutured vessels, (2) the incidence of thrombus formation, (3) hemorrhage, (4) the fate of the suture line, (5) the gross pathology, and (6) the microscopic pathology.

1. *Intraluminal pressures tolerated by sutured vessels.* When 6-0 braided silk and 5-0 medium chromic catgut were employed as the suture material, irrespective of the stitching technic, all sutured vessels withstood intraluminal pressures in excess of physiological needs. When 5-0 plain catgut was employed, on the other hand, with an everting mattress stitch dehiscence was inclined to occur within the first week after the anastomosis was performed.

The endpoint in testing for leakage was that level of air pressure, measured in millimeters of mercury, at which juxta-anastomotic bubbles or subadventitial blebs of air were visible. Although in some instances it was difficult to determine from whence the leak occurred, in most tests air appeared to emerge from the point of penetration of a suture. In no instance was leakage noted along the apposed tissue margin of the cut ends of the anastomosed area, nor did enormous or total dehiscence occur under the conditions of this examination.

2. *The incidence of thrombus formation.* In reporting the presence or absence of thrombi complete objectivity was adhered to regardless of any investigator's impression as to its potential clinical significance. The slightest evidence of thrombus formation, be it only a one-millimeter-in-diameter

* This occurred at 270 mm. of mercury on the seventh postoperative day.

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FIG. 5

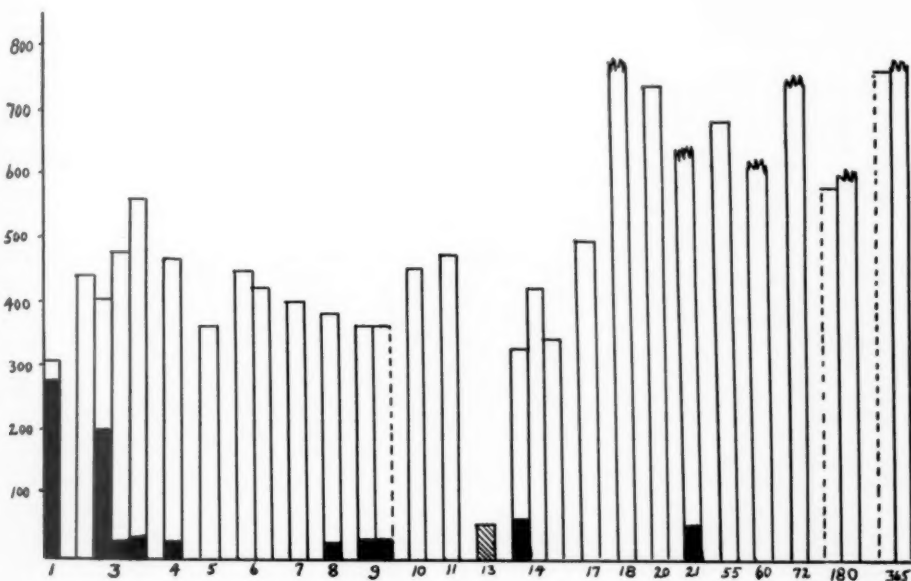
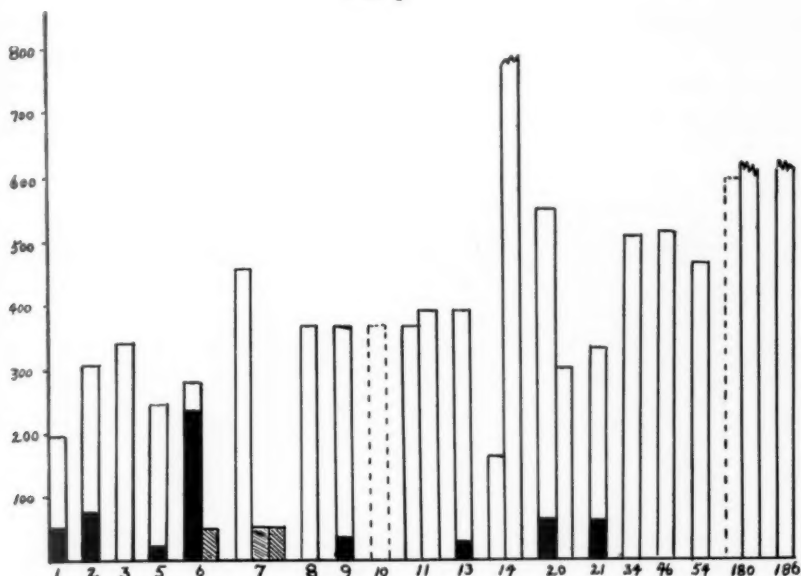


FIG. 6

FIG. 5.—Eversion type mattress suture with 6-0 silk. Numbers represent postoperative days. Each bar represents one anastomosis and pressure withstood. Shaded area represents occurrence and estimate of size of thrombus. Broken bar represents maximal pressure not determined. Diagonally lined bars represent hemorrhage. Dotted line bars indicate specimen not tested.

FIG. 6.—Continuous end-on coaptation suture through all layers with 6-0 silk. Numbers represent postoperative days. Each bar represents one anastomosis and pressure withstood. Shaded area represents occurrence and estimate of size of thrombus. Broken bar represents maximal pressure not determined. Diagonally lined bars represent hemorrhage. Dotted line bars indicate specimen not tested.

FIG. 7

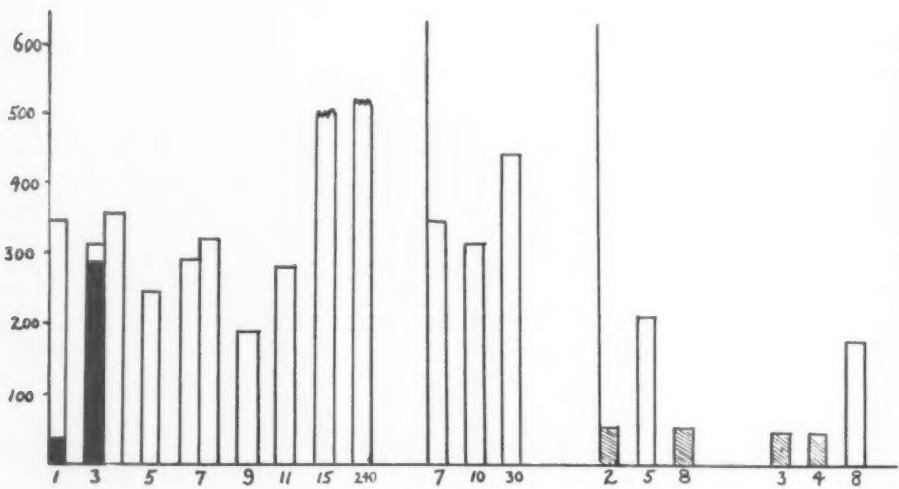
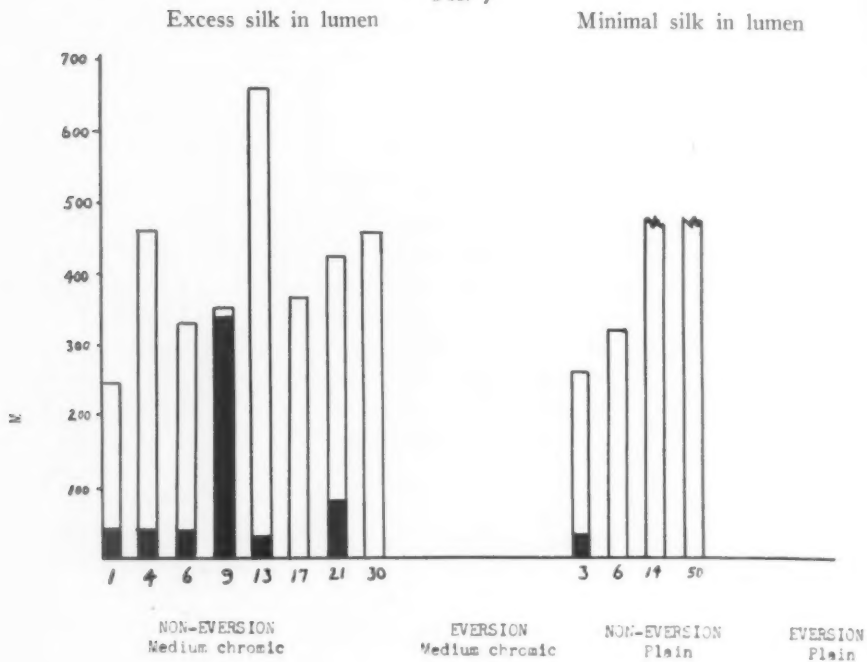


FIG. 8

FIG. 7.—End-on coaptation with 6-0 silk suture avoiding intima and with excess silk in the lumen. Numbers indicate postoperative days. Each bar represents one anastomosis and pressure withstood. Shaded area represents occurrence and estimate of size of thrombus. Broken bar indicates maximal pressure not determined.

FIG. 8.—Anastomosis with 5-0 medium chromic catgut and 5-0 plain catgut. Numbers represent postoperative days. Each bar represents one anastomosis and pressure withstood. Shaded areas represent occurrence and estimate of size of thrombus. Diagonally lined bar represents hemorrhage.

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accumulation of fibrin beneath or close to a suture, was tabulated positively (Figure 9). It is of interest to note that in only two instances were thrombi large enough to fill an entire vessel lumen.

In 30 non-everting, end-on anastomoses made with 6-0 braided silk taken through all layers of the vessel wall at one millimeter distance from the cut

FIG. 9

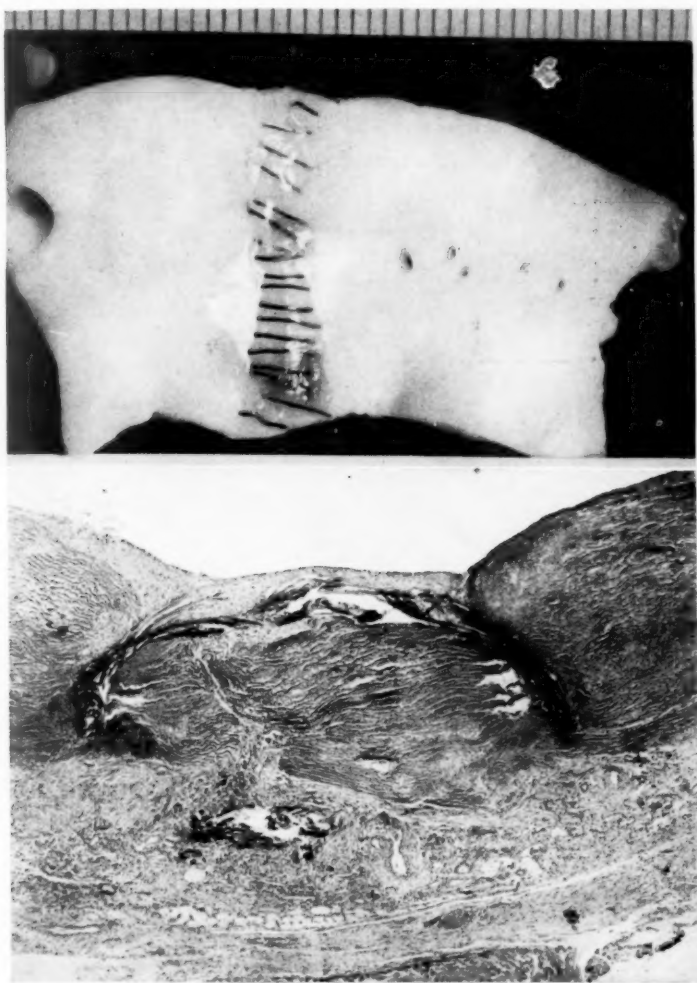


FIG. 9A

FIG. 9.—End-on coaptation through all layers with silk. Two weeks.
FIG. 9A.—Photomicrograph of specimen shown in Fig. 9. $\times 30$.

ends, there were four minute thrombi consisting of a mere fleck of fibrin; six instances of small to medium sized thrombi; and a large sized one in which the vessel lumen was occluded. In 26 everting anastomoses made with

6-0 braided silk there were seven specimens with small to medium sized thrombi and an additional three displaying only tiny fibrin flecks. In the eight dogs with non-everting end-on anastomoses, and with the silk placed two and a half millimeters from the cut edges to expose more silk in the lumen, there was one specimen with a medium sized thrombus (Figure 15) and three others which had minimal thrombotic deposits. Little or no silk was exposed in the lumen of four dogs in which stitches were taken through only the media and adventitia; only one of these four animals exhibited a tiny fleck of fibrin.

In the ten non-everting end-on anastomoses, made with 5-0 medium chromic catgut, there was one specimen with a medium sized thrombus and one with an enormous thrombus completely occluding the lumen. In no other experiment was there thrombus formation.

TABLE VI.—End-on Coaptation with 5-0 Medium Chromic Catgut Through All Layers

Dog No.	P.O. Day Leaking		Gross Findings
	Sacri-ficed	Pressure in mm. of Hg.	
21A	1	340	Small thrombus consisting of fibrin strands along one part of suture line.
52	3	310	Thrombus 2 cm. long completely filled lumen of vessel.
20A	3	358	No thrombus.
19A	5	230	No thrombus.
16A	7	290	No thrombus.
17A	7	320	No thrombus.
16A	9	190	No thrombus.
18A	11	290	No thrombus.
15A	75	No leak at 500	No thrombus.
14A	240	No leak at 500	No thrombus.

TABLE VII.—End-on Coaptation with 5-0 Plain Catgut Through All Layers

Dog	P.O. Day Leaking		Gross Findings
	Sacri-ficed	Pressure in mm. of Hg.	
62A	7	340	No thrombus.
61A	10	310	No thrombus.
54A	30	No leak at 450	No thrombus.

Thrombi forming during the first eight postoperative days, whether small, medium, or large, were soft and friable. Thrombi in animals surviving for longer periods of time were progressively firmer, and less easily dislocated. The thrombus shown in Figure 11 was discovered one year following the anastomosis, measured 10 x 5 x 3 mm. and had become an integral part of the vessel wall. In three instances unusual thrombi extended not only distally from the anastomotic line, but also several centimeters proximally into the subclavian artery.

No dog at any time displayed evidence of embolization clinically or at autopsy.

FIG. 10



FIG. 10A

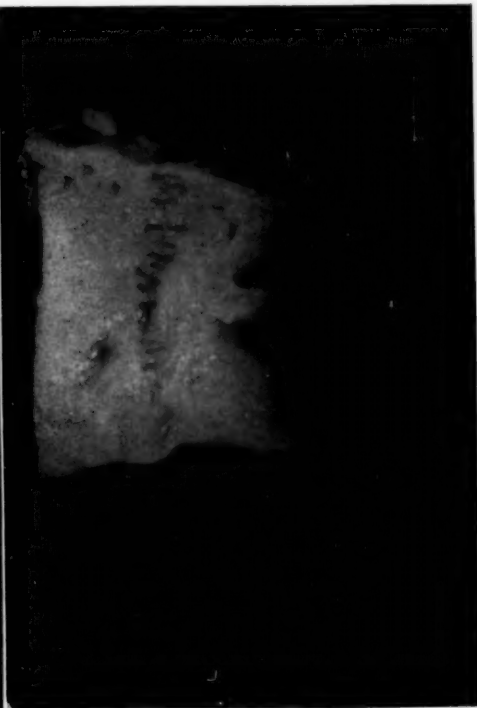


FIG. 11

FIG. 10.—End-on coaptation through all layers with silk. Eight weeks.
FIG. 11.—End-on coaptation through all layers with silk. One year.

FIG. 11A



FIG. 10A.—Photomicrograph of specimen shown in Fig. 10. x 30.
FIG. 11A.—Photomicrograph of specimen shown in Fig. 11. x 30.

3. *Hemorrhage.* Very little difficulty was encountered with acute blood loss at the time of surgery after some technical familiarity was acquired. When fatal hemorrhage occurred on the table (and it did in our early experience) these protocols have been omitted from this report. Rarely, a small leak resulted from a single untightened or misplaced stitch that failed to seal after five minutes of gentle pressure. In such instances the error was readily corrected by an additional interrupted suture. Even when stitches were properly placed an occasional spurt of blood emerged at the site of penetration of the needle; such bleeding consistently stopped in a few minutes with gentle digital pressure. Immediate hemorrhage did not appear in any way to be related to the type of suture material or the stitching technic.

TABLE VIII.—*Eversion with 5-0 Medium Chromic Catgut*

Dog No.	P.O. Day	Leaking Sacri- ficed	Pressure in mm. of Hg.	Gross Findings
67E	2	Died of hemorrhage		No thrombus.
19A	5		230	No thrombus.
57E	8	Died of hemorrhage		Gross dehiscence.

TABLE IX.—*Eversion with 5-0 Plain Catgut*

Dog No.	P.O. Day	Leaking Sacri- ficed	Pressure in mm. of Hg.	Gross Findings
64E	3	Hemorrhage		Gross dehiscence.
66E	4	Hemorrhage		Gross dehiscence.
65E	8		220	No thrombus.

For the most part delayed hemorrhage presented no serious problem. One instance of hemorrhage was encountered in a non-everting end-on anastomosis using silk. This animal died on the 13th postoperative day and examination of the specimen showed that at least one loop of the suture was improperly placed. In silk anastomoses performed with an everting stitch three fatal hemorrhages occurred—one on the sixth and two on the seventh postoperative days. In all three instances a loop of silk was noted to have pulled through the vessel, resulting in a focal dehiscence with hemorrhage.

With 5-0 chromic and 5-0 plain catgut sutures employing a non-everting end-on stitch no hemorrhage occurred. With an everting technic, on the contrary, fatal bleeding episodes were noted. Of three dogs sewed with 5-0 chromic catgut one bled on the eighth postoperative day; of three dogs sutured with 5-0 plain catgut one exsanguinated on the third and another on the fourth postoperative days. In the first instance one loop of mattress stitching pulled through and in the last two the suture material gave way and the vessels pulled apart completely.



FIG. 13

FIG. 12.—Everson with mattress type silk suture. Two weeks.
FIG. 13.—Everson with mattress type silk suture. Eight weeks.



FIG. 13A

FIG. 12A.—Photomicrograph of specimen shown in Fig. 12. $\times 30$.
FIG. 13A.—Photomicrograph of specimen shown in Fig. 13. $\times 30$.

4. *The fate of the suture material.* In every vessel, sewed end-on with silk and without eversion, the suture material remained intact, up to periods of one year (Figure 11). In several vessels united by silk and with eversion, individual loops of the suture were noted to have pulled through (Figures 13, 14)—a process that appears to continue throughout the late weeks and months of recovery as the eversion straightens out and the vascular fibers realign. In all instances in which the animals survived, the silk had become covered by a thin layer of endothelial cells as early as 10 to 16 days postoperatively. Of the 12 animals anastomosed with medium chromic catgut the suture material remained grossly visible up to 30 days, but none was recognizable after two months.

5. *The gross pathology.* When cylinders of the aorta, including the area of the anastomosis, were removed the site of suturing was usually surrounded by heaped up adventitia. Once this was carefully trimmed away a

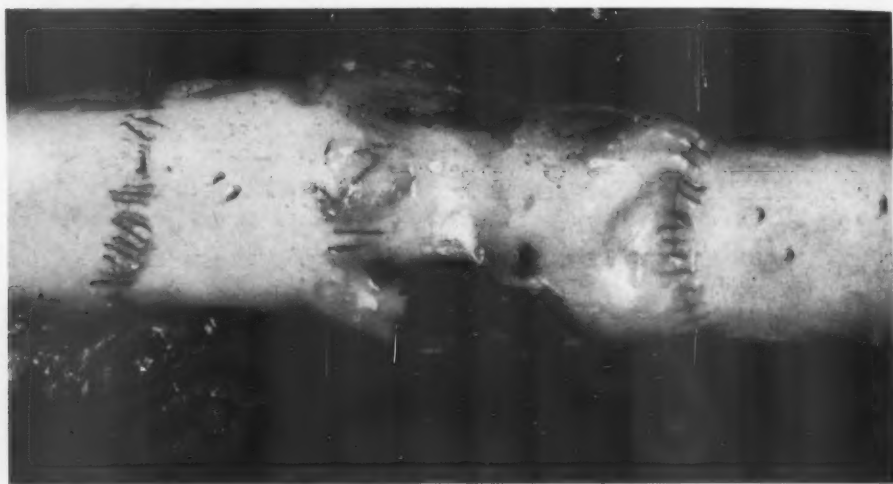


FIG. 14.—Specimen showing two lateral anastomoses made with end-on coaptation suture through all layers; central anastomosis made with everting mattress type suture. Six months.

slight stenosis was observed. Anastomoses which were performed a year previously on small puppies displayed a retarded growth compared with the adjacent vessel. In no experiments, however, had the outside diameter become lessened with the passage of time. There was little difference in the external appearance of specimens sutured several months earlier by various methods and with different materials.

After opening the cylinders longitudinally the specimens were pinned on a board to facilitate careful scrutiny. Vessels anastomosed with non-everting end-on silk sutures, taken through all layers, uniformly displayed a smooth intimal apposition (Figures 16, 17). When the intima was omitted from the suture a wider slit occurred between apposing intimal margins. Vessels anastomosed with a continuous everting silk mattress suture con-

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sistently displayed a more irregular apposition and a furrow occurred at the everted interface (Figure 12). With the passage of time postoperatively, the prominence of this sinuate track became less noticeable, but small pits regularly developed where mattress stitches had pulled through (Figures 13, 14). The smoothest endothelial surfaces were observed where non-everting catgut sutures were employed.

6. *The microscopic pathology.* Reference to Figures 12A and 13A best demonstrate how the fibers of the media bend outwards in the early stages of repair where everting stitches were employed. After several months of healing these fibers gradually become realigned parallel with the long axis of the aorta. During such intervals of time the intervening cleft is filled with fibrin and proliferating intimal cells. Anastomoses performed with non-

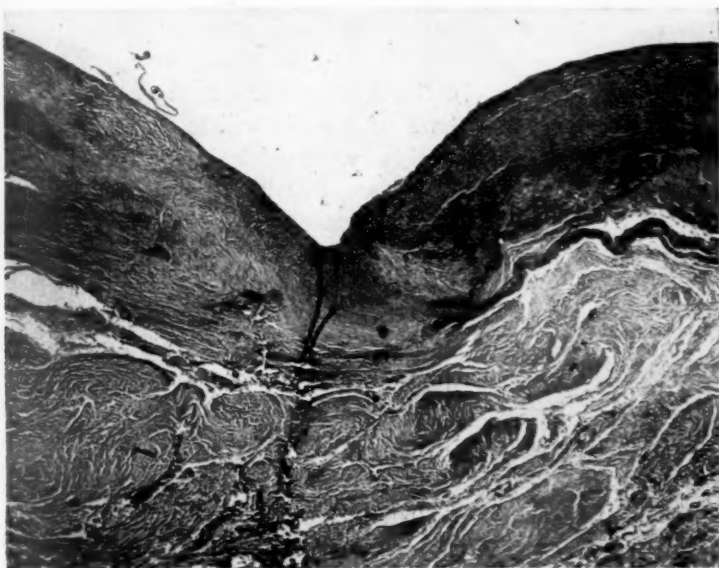


FIG. 14A.—Photomicrograph of middle anastomosis shown in Fig. 14.
x 30.

everting end-on stitching, on the other hand, are anatomically aligned at once (Figure 10A), with final healing occurring earlier than after suturing with eversion. In all types of stitching the sutures become rapidly mesothelialized, and in a very few days these cells (Figures 9A and 12A) migrate across the fibrin base. Chromic catgut sutures are demonstrable in microscopic sections up to 60 days, but become largely fragmented, absorbed, and replaced with fibrous scar tissue soon thereafter.

DISCUSSION

This study suggests that in dogs the divided thoracic aorta, when united either with a continuous non-everting end-on whipping stitch or with an everting continuous mattress stitch, employing 6-0 braided silk, is consistently strong enough to withstand more than the physiological needs of the

animal. As the severed aorta heals, the everting mattress stitch tends to pull through the vessel wall, the eversion tends to flatten out, and in this manner the longitudinal fibers realign. Should the mattress loop of the suture pull through during the first seven days, fatal hemorrhages may occur. If the sutures pull through later, the healing has usually progressed far enough so that no hemorrhage ensues; when, however, the suture has pulled through at a late stage foveolae or crypto-aneurysms are formed which result in an intraluminal irregularity of the endothelial lining. As each anastomotic line was developed, a snug but in nowise strangulating tension was maintained on the laid sutures.

The presence of intraluminal or subendothelial loops which have cut through, as well as imperfections of the aortic wall, may be related to other factors. All anastomoses derive strength by the acceptance at numerous points of a fraction of the total strain. This distribution of tension may be less equitable with the everting type than with the non-everting end-on whipping stitch including all layers. In the former, focal areas might be compelled to accept a disproportionate share of the disrupting force. Another possibility stems from the shearing action generated by each cardiac thrust which would ultimately saw through the segment of aortic wall captured by a particular loop of mattress suture. Support for these theoretical considerations is provided by a special experiment designed to explore this problem further.

In this dog an everting type mattress suture anastomosis was made after transection of the aorta. Six months later this anastomosis was resected* removing 1 cm. of aorta on each side of the anastomotic line. An end-on anastomosis without eversion was made with an over-and-over whipping stitch of 6-0 silk through all layers. Two weeks following this the dog was reoperated upon, the aorta divided distal to the anastomosis, and a fresh homo-graft 10 mm. longer than the resected segment was inserted to bridge this defect. The proximal anastomosis on the graft was effected with a 6-0 silk everting type of mattress suture and the distal anastomosis made with a 6-0 silk over-and-over whipping stitch including all layers. Six months later the entire aorta was removed and examined. As noted in Figure 14 the outside anastomoses are of the end-on whipping stitch variety, and the middle suture line is of the everting type. There appears to be more evidence of dislocation in the latter (free loops and pitted walls) than in either of the other anastomoses, despite the fact that the proximal one was under considerably more tension. At the time it was made, a 2 centimeter segment had just been excised whereas a 3 centimeter graft had just been added upon the occasion of the last procedure.

That everting sutures suffer more from tension on the line of anastomoses was also demonstrated by a short series of experiments in which either a chromic or a plain catgut suture was employed. The high incidence of fatal

* This anastomosis demonstrated free loops where the mattress stitching had pulled through.

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FIG. 16

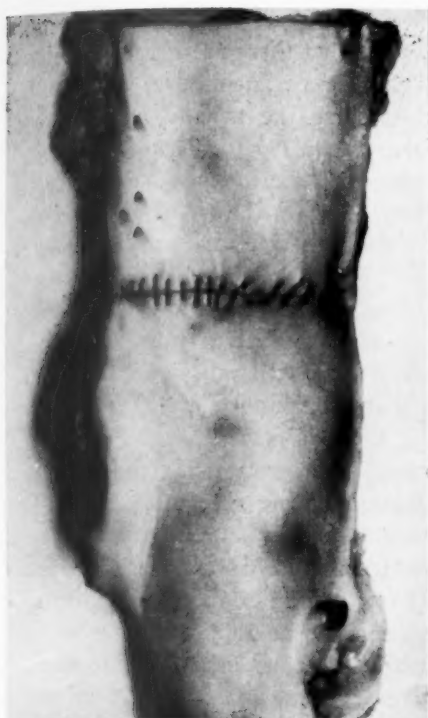


FIG. 15



FIG. 17A

FIG. 17

FIG. 15.—Medium sized thrombus in anastomosis made with excess silk exposed to the lumen. Three days.

FIG. 16.—End-on coaptation through all layers made with 5-0 medium chromic catgut. One week.

FIG. 17.—End-on coaptation with 5-0 medium chromic catgut through all layers. 75 days.

FIG. 17A.—Photomicrograph of specimen shown in Fig. 17. $\times 30$.

hemorrhages in the catgut everted series (three out of six) compared with the end-on non-everting series (none), suggests that there are greater tension effects on the suture line with eversion. These experiments are, in a sense, peak load tests of healing capacity. But, since the usually encountered hyperpiesia is considerably below the pressure required to disrupt an everting type of anastomosis, any broad claims for superiority of the end-on whipping type stitch appear rather academic.

As far as thromboses are concerned these experiments corroborate the results of other workers: any irregularity in or on the vessel wall promotes thrombus formation. In our experience, this does not appear to be simply a question of the presence or absence of non-absorbable suture material. Smith⁴ has shown that if a fine silk suture is threaded transversely through an artery, tiny clots form in the center of the turbulent stream. These grow until the vessel becomes occluded. When a stitch is placed parallel with the longitudinal axis of the vessel, the foreign body hugs the intima, turbulence is minimal and few thrombi form. Examination of the specimens from this series of experiments suggests that the irregularities at the anastomotic line are probably as important in thrombus formation as the suture material used.

The incidence of thrombus formation along the anastomotic site in these experiments was nearly the same whether suturing was done with an everting or a non-everting stitch. Thrombus formation was infrequent when end-on stitching was carried out to include adventitia and media, but omitting the intima.

Catgut anastomoses have uniformly produced the smoothest end results when a non-everting end-on stitching was carried out. Yet, because of lower pressures at which leaking occurred in the early days of healing, catgut anastomoses offer a reduced margin of safety.

CONCLUSIONS

1. The severed thoracic aorta of the dog, united with 6-0 braided silk, using an end-on whipping stitch or an everting mattress type of suture, has tensile strength in excess of the animal's physiologic needs.
2. When the eversion type of mattress sutures pulls through the vessel wall, irregularities develop on the endothelial surfaces and sometimes in the structure of the vessel wall.
3. A continuous 6-0 braided silk placed with a non-everting end-on coaptation stitch remains intact in vessels observed up to one year post-operatively.
4. There appears to be an equal incidence of thrombus formation in anastomoses made with over and over whipping stitch with 6-0 silk without eversion and in anastomoses made with 6-0 silk of the everting mattress type.
5. Intraluminal silk plays a small role in thrombus formation at the anastomotic line.
6. There was no instance in which the anastomosis became narrower than at the time of surgery. In anastomoses done on puppies, nevertheless, it was

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noted that growth at the site of suturing does not keep abreast of the growth of the adjacent aorta.

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THE SURGICAL RELIEF OF CONGESTION IN THE PULMONARY CIRCULATION IN CASES OF SEVERE MITRAL STENOSIS*

PRELIMINARY REPORT OF SIX CASES TREATED BY MEANS OF ANASTOMOSIS
BETWEEN THE PULMONARY AND SYSTEMIC VENOUS SYSTEMS

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IT IS ESTIMATED that approximately ten per cent of patients with rheumatic disease of the mitral valve ultimately develop a preponderant degree of stenosis. Although such patients may not, at least for many years, experience any striking symptoms or suffer any great limitation of their activities, there are some who develop a syndrome which is characterized by the occurrence of attacks of pulmonary edema. These attacks are precipitated by the physiologic changes which occur during menstruation or pregnancy, intercurrent infections, fever, or tachycardia induced by emotional disturbances or marked increases in physical exertion. But for many years the heart itself may remain relatively normal save for slight enlargement.

The explanation for the phenomenon depends upon the concurrence of two factors. The first is that as a result of the long-standing mitral stenosis, a continuous increase in the pressure within the pulmonary circulation develops. With this increased pressure the characteristic congested condition of the lungs becomes established. The second factor is that the right ventricle ultimately becomes hypertrophied in response to the increased pressure in the pulmonary circuit. The result of this is that under conditions of stress the strong right ventricle forces blood into the lungs so as to increase greatly the already elevated pressure within the pulmonary vessels. This inevitably results under strain in the transudation of fluid and often of blood into the pulmonary alveoli, producing the clinical picture of pulmonary edema. After the stage of the disease is reached when attacks of pulmonary edema occur with frequency, the patient lives in jeopardy and is forced to adopt a program of very limited activity even though the heart muscle remains competent. Such patients often die of pulmonary failure rather than from failure of the heart itself.

The first attempts to relieve the effects of tight mitral stenosis were directed chiefly at the enlargement of the mitral opening. Originally this was done by dilating the stenosed orifice with a finger inserted through a small incision in the right ventricle. Later an effort was made by Cutler¹ and others to enlarge the opening by means of cutting instruments. These early attempts met with failure, and the experiences of others since then have been for the most part equally unsuccessful. Recently Harken² has modified the technic

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of valvulotomy and has had somewhat better results. It must be kept in mind, however, that in addition to the rather considerable mortality risk of the procedure, the operation leaves the patient with an increase in the element of regurgitation which cannot be controlled. The unfavorable effects of this factor upon the heart muscle may lead to a disappointing end result.

The interesting observation first reported by Lutembacher,³ that patients with tight mitral stenosis who have a coexisting patent interauricular septal defect do not usually suffer from paroxysms of pulmonary edema, has led to the suggestion that such a defect might be created by surgical means. Blalock has begun to approach the problem from this angle and has published the details of his technic as utilized in experimental animals.⁴ This operation of course involves the serious risk of manipulations within the heart itself.

A clue to the possibility that a different approach to the problem of relieving the congestion within the pulmonary circulation may exist arises from the observation that in patients with tight mitral stenosis the bronchial veins become enormously dilated. This increase in the collateral bronchial venous circulation tends to provide an outlet, limited in extent to be sure, from the congested pulmonary vessels. This compensatory mechanism suggests that if a larger communication can be created between the pulmonary and the systemic venous systems, a more effective relief of sudden increments of pressure within the pulmonary circuit might be provided. Such a shunt, in addition to being an improvement upon nature's spontaneous efforts to create a collateral communication, would also have essentially the same effect upon the pressure in the congested area as that which results from the presence of an interauricular septal defect. It would, in fact, be essentially equivalent to the creation of a septal defect, but would have the advantage that it is an operation performed outside of the heart. The risk of intracardiac manipulation would thereby be avoided.

OPERATION—ANASTOMOSIS BETWEEN THE SUPERIOR SEGMENT BRANCH OF THE RIGHT INFERIOR PULMONARY VEIN AND THE AZYGOS VEIN

Anatomical considerations. Two veins exist which are ideally suited for the creation of a shunt from the pulmonary to the systemic circulation. These are the superior segment branch of the right inferior pulmonary vein and the azygos vein. These veins lie close together and have approximately the same diameter. Furthermore, their direction is nearly enough parallel to make it easy to approximate them end-to-end after division. From the mechanical aspect also the release of pressure in the left auricle, which might result from an anastomosis between the cardiac end of the pulmonary vein and the cardiac end of the severed azygos vein, would seem to produce the desired effect upon the congestion in the lungs (Fig. 1).

The azygos vein arises over the bodies of the upper lumbar vertebrae and enters the thorax through the aortic hiatus in the diaphragm. It passes along

the right side of the vertebral column to the level of the fourth thoracic vertebra where it arches forward over the right main bronchus to enter the superior vena cava. In its course it lies near the esophagus and next to the thoracic duct. It is joined by the hemiazygos and accessory hemiazygos veins, the right intercostal veins, the right highest intercostal vein, the esophageal, mediastinal, and pericardial veins, and the right bronchial vein. Its diameter varies from 2 to 3 millimeters at its lower end to 6 or 7 millimeters or more at its termination in the superior vena cava. There are, of course, variations in size from one person to another. The superior segment branch of the right inferior pulmonary vein arises in the superior segment of the right lower lobe behind the corresponding segmental bronchus. During its short course before it joins the veins from the basal segments of the lower lobe to form the

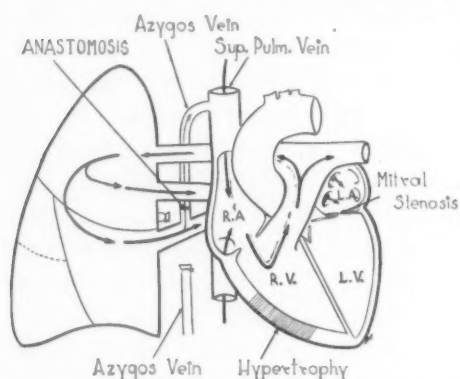


FIG. 1.—Pulmonary-azygos venous shunt. Schematic diagram to show the mechanical effect of a shunt between the pulmonary and the systemic venous circulations produced by an anastomosis between the azygos vein and the right inferior pulmonary vein. Arrow shows that some of the blood in the inferior pulmonary vein is forced by the high pressure in the pulmonary circuit to enter the azygos vein through the shunt, thus relieving to some extent the excess of pulmonary pressure.

inferior pulmonary vein, it receives several small branches, some of which may enter it close to its termination. Occasionally the superior segmental vein enters the left auricle independently of the inferior pulmonary vein as a separate trunk. Its diameter varies from approximately 3 to 5 millimeters. In patients with mitral stenosis this vein, in company with all the pulmonary veins, is somewhat larger in diameter than normal and unusually turgid because of the increased pressure in the left auricle. It is thin-walled, however, and corresponds in this respect with the azygos vein to which it is to be anastomosed.

Special Precautions To Be Observed. Because of the danger of inducing an attack of pulmonary con-

gestion as a result of excitement, the patient is put to sleep in his room by means of Pentothal injected intravenously. He is then moved to the operating room and the inhalation anesthesia is begun while he is still asleep. Ether mixed with oxygen is administered through an intratracheal tube. During the progress of the operation the anesthetist must be ready at all times to aspirate secretions from the trachea. It is well also for the surgeon to work with the lung expanded as much as possible.

If the amount of secretion coming from the trachea should increase to the degree where it suggests the onset of excessive pulmonary congestion during the operation, tourniquets should be applied quickly by an assistant to all four extremities. It is wise to be prepared also for the performance of a venesection

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in case of emergency, but this procedure has not been necessary in any of the six patients operated upon to date.

Although it is necessary to have an infusion of dextrose solution running into a vein in case of emergency, the rate of flow must be slow. Blood is not used but should be available for use in case of hemorrhage.

Technic. With the patient lying on his left side, his right side arched slightly so as to widen the intercostal spaces, a standard thoracotomy incision is made. The pleural cavity is opened through the sixth intercostal space (or through the bed of the sixth rib if the rib resection technic is adopted). The wound edges are covered with pads of gauze moistened in sterile saline solution and a rib spreader is inserted. The lung is held forward by the hand of the first assistant and the pleura is reflected from the inferior pulmonary vein. The superior segment branch of this vein is identified and freed from the surrounding areolar tissue by sharp and blunt dissection. Any small tributaries which may be found must be ligated with fine silk and divided. The vein is followed upwards into the lung as far as its origin where two or three fairly large tributaries join beneath and slightly anterior to the lower portion of the superior segment bronchus. The vein is not divided until the freeing of the azygos vein has been accomplished (Fig. 2).

The mediastinal pleura and retropleural fascia over the azygos vein are incised longitudinally. The azygos vein is freed from a point 2 or 3 centimeters below the level of the superior segmental vein upwards as far as its junction with the highest intercostal vein. In freeing the azygos vein it is usually necessary to ligate and divide a large number of its tributaries. These include the accessory hemiazygos, sometimes the hemiazygos, most of the right intercostal veins above the level of transection of the azygos vein, and many small esophageal and other mediastinal branches. Occasionally in order to gain sufficient length for the performance of the anastomosis, it may be necessary to divide the right highest intercostal vein. This was necessary in two of the six cases.

A short clamp, "bulldog" type, is applied to the superior segment vein as closely as possible to its junction with the basal segment branches of the inferior pulmonary vein. A hemostatic forceps is then applied as far into the lung as necessary to avoid sacrificing any of its length and the vein is cut close to the hemostat. A suture ligature of heavy silk is used to tie the pulmonary end of the vein. A bulldog clamp is placed across the azygos vein at the upper limit of the dissection and the vein is ligated and divided at the lower limit approximately 2 centimeters below the level of the pulmonary vein (Fig. 3).

The blood is flushed out of each of the severed veins with saline solution, using a blunt needle attached to a small syringe. A Blakemore-Lord vitallium tube having a diameter of proper size to permit cuffing back the azygos vein on it is then applied to the upper or cardiac end of the azygos vein. The end of the azygos vein is passed through the tube and turned back to the ferrule

near the flange where it is tied with heavy silk. Three strands of arterial silk suture material are passed through the end of the pulmonary vein at equidistant points. Short hemostatic forceps are fastened to these strands about 2 inches from the end of the vein. A curved hemostat attached to the

FIG. 2

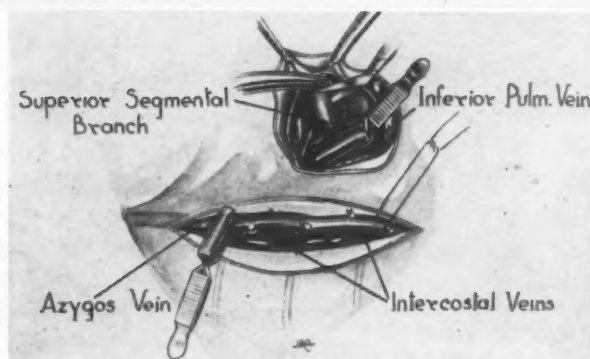
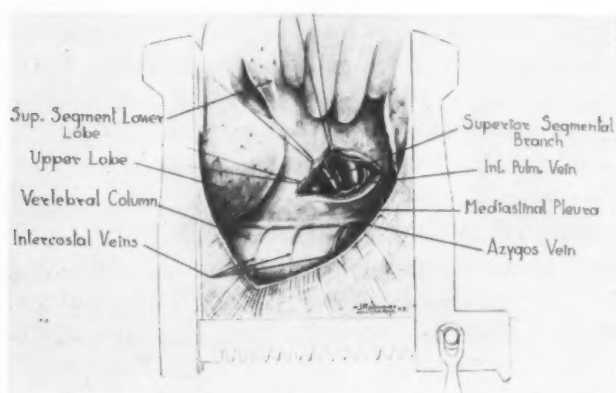


FIG. 3

FIG. 2.—Drawing made at operation (Case 3) to show the superior segmental branch of the inferior pulmonary vein after completion of the dissection but before it has been severed. Azygos vein shown before dissection.

FIG. 3.—Drawing showing the completed dissection of both veins as they are about to be cut across. The bulldog clamps are in correct position. Ligature on the azygos vein ready to be tied preparatory to division approximately 2 cm. beyond the level of the pulmonary vein. Hemostat in place on the superior segmental branch of the inferior pulmonary vein preparatory to division with fine straight scissors.

flange of the tube is used to hold the end of the azygos vein and direct it into the open end of the pulmonary vein which is drawn over it by exerting traction on the three strands of silk. The pulmonary vein is drawn up over the proximal ferrule on the tube where it is held with a silk tie. A second

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ligature is then applied to hold the veins together close to the tip of the tube in the manner described by Blakemore and Lord.⁵ (Fig. 4.)

The bulldog clamp is removed from the azygos vein first and then that from the pulmonary vein. In a moment the blood can be observed flowing briskly from the high pressure area in the pulmonary vein to the low pressure region in the azygos vein. Palpation of the latter beyond the anastomosis reveals the presence of a soft thrill.

A small incision is made in a lower intercostal space posteriorly and a large catheter is inserted for drainage. The lung is then expanded fully and the chest wall is closed.

The Blakemore-Lord non-suture method of anastomosis was chosen in preference to the suture method for two reasons. In the first place it avoids the presence of suture material in the intima of the veins and tends to minimize the danger of thrombosis. This danger may be more theoretical than actual, but it is not known how long a swift flow of blood will persist through the shunt, which is the only factor beyond the use of anticoagulants which can be depended upon to overcome a tendency to thrombosis. In the second place, the two veins which are used for the anastomosis are exceedingly fragile and small in diameter so that the suture method would be unusually difficult. Experience with the Blakemore-Lord tube method in the six cases reported seems to indicate that there is no reason to abandon its use.

OBSERVATIONS AT OPERATION

Appearance of the lung. In all six patients operated upon thus far the lung has shown a characteristic appearance. The color is dusky, not exactly cyanotic but rather suffused with a purplish red hue. It is unusually firm but becomes atelectatic quickly when the intrapulmonary pressure is released. This suggests that the firmness is due to the increased tension in the large pulmonary vascular bed rather than in the alveolar substance. There is always also marked dilatation of the bronchial and perihilar collateral veins. The pulmonary veins themselves are dilated, firm, and pulsatile.

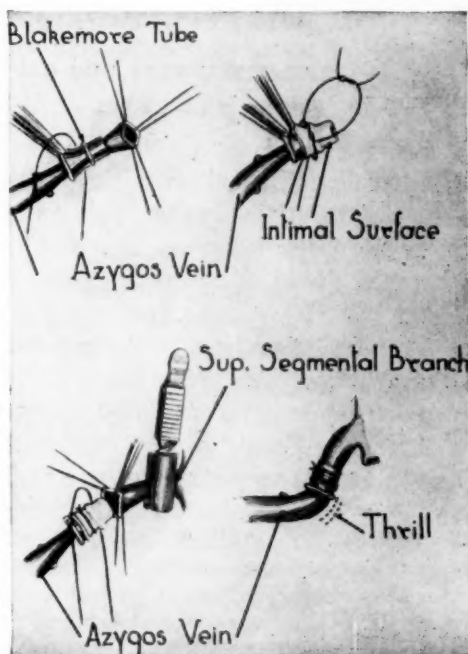


FIG. 4.—Drawing to show the several steps in the performance of the anastomosis by the Blakemore-Lord non-suture method as applied to the union of the azygos vein with the superior segmental branch of the inferior pulmonary vein. Completed anastomosis shown with location of thrill felt after the bulldog clamps have been removed.

Appearance of the heart. The heart appears essentially normal except for the very tense dilated left auricle which can be seen bulging posteriorly and to the right into the field of operation.

Appearance of the Superior Segment of the Lower Lobe after Ligation of Its Vein. At the completion of the operation, the superior segment of the lower lobe has been observed in all cases to assume a dusky, dull red or purple color. In one patient (Case 5) who was on the verge of congestive failure during the course of the operation, this segment of the lung was actually hemorrhagic in appearance. These observations are consistent with the findings of Swan and Mulligan in experimental animals after ligation of the pulmonary veins.⁶

EXPERIENCE WITH THE OPERATION—SIX CASE REPORTS

An anastomosis between the superior segment branch of the inferior pulmonary vein and the azygos vein has been performed in six patients with so-called "pure" mitral stenosis. Two of these were operated upon too recently for a satisfactory evaluation of the result. One died of an exacerbation of the rheumatic fever infection. The first three, however, have been enormously improved. None of these patients has ever experienced an attack of pulmonary edema since leaving the hospital. All three had been forced to adopt a life of semi-invalidism before the operation. Two of them were actually unable to carry on outside the hospital. All three are now leading normal lives after a prolonged period of disability before the operation was performed.

Complete details of the case histories are to be reported elsewhere.⁷ Brief abstracts are submitted here as follows:

Case 1.—Mrs. O. C. B. (MGH 610979), 17-year-old mulatto girl, had rheumatic fever at age 5. Diagnosis of mitral stenosis was made at age 14. First attack of pulmonary edema occurred at age 15, and thereafter she experienced numerous attacks with cough, orthopnea, wheezing, and expectoration of blood-streaked sputum. The attacks occurred often during menstrual periods. One attack almost resulted in death. At this time she was in an oxygen tent for 4 days. Between attacks she experienced dyspnea, and was forced to give up school. She was admitted finally to hospital where she had several slight attacks even under treatment with digitalis, low sodium diet, and diuretics.

Examination revealed a slight cardiac enlargement, with a characteristic murmur of mitral stenosis. Electrocardiogram was normal, save for right axis deviation. There was no evidence of right side cardiac failure.

Operation. March 23, 1948. The lung was characteristically dusky, not adherent. The superior segment vein was short (not over 1 cm.). The azygos vein was slightly larger than the superior segment vein in diameter. A Blakemore-Lord tube non-suture anastomosis was performed. The flow of blood through the shunt was excellent. A thrill was felt.

Pressure in the left auricle before making the anastomosis was 460 mm. of water. It was not thought wise to take the additional time at the end of the operation for a pressure reading after completion of the anastomosis.

Subsequent Course. Her immediate recovery was rapid and uncomplicated. She was allowed out of bed on the third postoperative day. Since her discharge from the hospital she has led an unusually active life and has had no attacks of pulmonary edema. On

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one occasion, in August, 1948, she was admitted to the hospital with an attack of gonorrheal peritonitis with a fever of 103°F. It was discovered also that she was pregnant, and after a favorable response to penicillin therapy, she had an abortion (therapeutic) done. Her lungs remained dry throughout this illness. In January, 1949, she was admitted once again for interruption of a second pregnancy. No evidence of pulmonary edema was observed at this time.

Case 2.—M. Z. (MGH 624098), 27-year-old male, entered July, 1948, because of recurring attacks of pulmonary edema. There was a diagnosis of rheumatic heart disease at age 17. First episode of pulmonary edema occurred in 1945 at age 24. The attacks became frequent and increasingly severe. They were precipitated by emotional disturbances, physical exertion, or infections. Several had been almost lethal. Auricular fibrillation developed in May, 1948.

Examination. On entry there was moderate cardiac enlargement with absolutely irregular rhythm; rate 120; characteristic murmurs. Râles could be heard at both lung bases. Blood pressure 120/70. During a three months' residence in hospital before the operation he had attacks of pulmonary edema varying from mild episodes of nocturnal dyspnea and wheezing to attacks of such severity that it seemed unlikely that he would recover. For a long time his condition was considered to be too precarious to contemplate operation.

Operation. October 24, 1948. The operation as described was performed. The lung was tense and dusky in color. No pressure readings were made because of his precarious condition.

Subsequent Course. On the afternoon of the day of operation there was a transitory episode of pulmonary congestion. From that time on, however, he made a gradual but satisfactory recovery. He is now well and is touring the United States in anticipation of his return to his home in South America. He has had no attacks of pulmonary edema since the day of operation.

Case 3.—Mrs. R. O. (MGH 638226), age 24, was admitted October, 1948. The first knowledge of any abnormality came as a result of an acute attack of pulmonary edema occurring during the course of a pregnancy in 1946 (age 22). Two other severe attacks had occurred since, one as a result of exertion, the other during an attack of "bronchitis." The last episode was the most severe and required treatment in a hospital. A fourth attack occurred just before entry. She had had a chronic cough for many months.

Examination. This revealed a small heart with characteristic auscultatory signs. Blood pressure 105/75. Electrocardiogram normal except for right axis deviation and prominent P waves. Cardiac catheterization with the patient at rest showed a pulmonary artery pressure of 46 mm. Hg. systolic over 25 mm. Hg. diastolic; pulse 95. After gentle exercise (one minute) it was 75/35; pulse 116. Developed pulmonary edema during the exercise test. (Normal 25 ± 5 to 5, with little change on exercise.)

Operation. November 18, 1948. The lung was not as dusky and firm as in Cases 1 and 2, but was distinctly abnormal. A very satisfactory anastomosis was made between the superior segment vein and the azygos vein. Pressure readings from the left auricle were 425 mm. of water before the anastomosis and 390 mm. of water after its completion.

Subsequent Course. Her recovery was uncomplicated. Her cough disappeared. Has had no attacks of pulmonary congestion even during a severe upper respiratory infection. Cardiac catheterization on February 19, 1949, revealed a pulmonary artery pressure of 50 mm. Hg. systolic and 20 mm. Hg. diastolic; pulse 78 at rest. The pressure after one minute of exercise was 65 mm. Hg. systolic and 25 diastolic; pulse 95.

Case 4.—D. G. (MGH 649017), age 42, female. Admitted January 21, 1949. She had rheumatic fever at age 14. Her first symptom referable to the heart was exertional

dyspnea noticed during her second pregnancy at age 34. The first severe attack of pulmonary edema occurred after exertion at age 38. At that time she had dyspnea and blood-tinged frothy expectoration. Diagnosis of mitral stenosis made at that time. From that time she experienced rapid progression of difficulty with frequent episodes of pulmonary edema. During the past year she had been forced to give up almost all normal activities and had experienced frequent attacks of pulmonary edema. She was hospitalized three times because of the severity of attacks. There was a history of transient left hemiplegia two and one-half years before admission. During the past four years she had been taking digitoxin and quinidine with regularity because of the tendency of her heart to develop auricular fibrillation.

Examination. The auscultatory signs were characteristic of mitral stenosis. No evidence of enlargement. Blood pressure 100/60; pulse 88; normal rhythm. Cardiac catheterization revealed a pulmonary artery pressure after a period of rest of 40 systolic and 10 diastolic with a pulse of 78. After exercise the pulmonary artery pressure rose to 104 systolic and 40 diastolic with a pulse rate of 100.

Operation. (January 31, 1949.) The lung was not as congested and cyanotic in color as in the other cases and there was much less evidence of increased collateral circulation around the hilum of the lung. The usual anastomosis was made and on release of the clamps the blood began promptly to rush through the anastomosis into the azygos vein and the function of the shunt was very satisfactory. Pressure readings were taken and it was noticed that after this procedure the flow of blood through the anastomosis was nowhere near as great as it had been before and it was quite obvious that it is unwise to occlude the vein even temporarily after the anastomosis has been made.

Subsequent Course. Postoperative course quite satisfactory except for moderate pulmonary edema on second postoperative day. The patient was treated with oxygen, morphine, mercuhydrin. She developed a pulmonary embolus on sixteenth postoperative day. A bilateral superficial femoral vein ligation was performed in an effort to prevent other emboli. Convalescence was uneventful thereafter, and patient was discharged from hospital on February 26, 1949. Postoperative pulmonary artery pressure determinations will be made in the near future.

Case 5.—A. P. (MGH 106907), age 30, female. She had no history of rheumatic fever, but a diagnosis of mitral stenosis was established at age 19. She first noticed dyspnea on exertion and orthopnea at age 25 during pregnancy. During the sixth month of her pregnancy she experienced a very severe attack of pulmonary edema, because of which the pregnancy was interrupted by cesarian section. Since then she had experienced rapid progression of difficulty, with frequent attacks of pulmonary edema, often several mild attacks per day. She had subacute bacterial endocarditis 16 months before admission which responded favorably to treatment with penicillin.

Examination. There was no venous distention, but scattered inconstant fine inspiratory basal rales. Dullness and diminished breath sounds at right base posteriorly suggesting fluid. Her heart was markedly enlarged to the left, with a maximum palpable impulse in the midaxillary line, fifth interspace. There was a loud, grade III to IV mid-diastolic murmur over entire precordium and left back, loudest at apex. Venous pressure in the left forearm was 123 mm. of water. Vital capacity was 1.8 liters (57 per cent of normal). Pulmonary artery pressure was 110/30 mm. of mercury at rest, with pulse of 95, and 145/65 after exercise, pulse 125.

Operation. (February 7, 1949.) An effusion of slightly turbid pleural fluid was found and 325 cc. was obtained on aspiration. The lung showed a very suffused, dull, purplish red appearance. There was a large development of collateral vessels throughout the hilum of the lung involving tissues between fissures and around bronchi and pulmonary vessels. The lung was unusually firm. The pleura was very much thickened and reddish in appearance, as though there had been inflammation present. Pressure within the auricle was 530 mm. of water. Anastomosis was performed without difficulty. Pressure

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reading following anastomosis was 379 mm. of water. The flow of blood through the shunt was unusually forceful. A marked thrill was felt in the azygos vein beyond the anastomosis.

Subsequent Course. An attack of pulmonary edema immediately postoperatively was relieved by tourniquets and morphine. Fever rose to 105 and 106.^o The postoperative course was extremely stormy, requiring oxygen, digitalis, aspirin, and frequent use of morphine and tourniquets for pulmonary edema. She gradually improved, but on the tenth day postoperatively developed tachycardia and pulmonary edema and died suddenly on the eleventh day. Autopsy revealed marked evidence of an exacerbation of rheumatic fever. There were fresh vegetations on the heart valves. The venous shunt was patent except for a recent (6 to 24 hour) thrombus in the pulmonary vein, probably a terminal occurrence.

Case 6.—E. R. (MGH 657333), age 27, female, was admitted March 31, 1949. There was a history of febrile illness suggesting rheumatic fever during childhood. Four years previously, she experienced a first attack of pulmonary edema with dyspnea and expectoration of frothy blood-tinged sputum. Subsequently she suffered similar attacks, especially during the previous year, with four severe episodes and several minor ones. She had a therapeutic abortion two months prior to admission.

Examination. Auscultatory signs were consistent with mitral stenosis, with only slight cardiac enlargement; lungs clear; pulse 76. Roentgen examination of the chest showed enlargement of left atrium. Vital capacity was 2.8 liters. Hemoglobin 14.4 Gm. per cent. Pulmonary artery pressure while resting was 41 mm. of mercury systolic and 18 diastolic, with pulse 75; after exercise 65 mm. mercury systolic and 28 diastolic, with pulse 98.

Operation (April 11, 1949). The lung showed the characteristic congested appearance; no adhesions; left auricle very large, pressing the esophagus to the right. The azygos vein was unusually small in diameter but a satisfactory anastomosis was made using a 3 mm. Blakemore-Lord tube. The flow of blood through the shunt was active. The pressure in the left auricle before the anastomosis was 460 mm. of water; after the anastomosis it was 370 mm. of water.

Subsequent Course. The patient has made an uneventful convalescence to date, but is still in hospital. It is too early for evaluation.

COMMENT

The clinical improvement in the first three patients since the performance of the operation has been striking. Their exertional dyspnea and palpitation have diminished. None has experienced any attacks of pulmonary edema even under the stress of illness, emotional strain, and considerable degrees of physical exertion.

It has been demonstrated on the operating table that the shunt produces a significant lowering of the pressure in the left auricle. In one case there was a drop from 425 to 390 mm. of water (or 8.2 per cent of the initial pressure). In another the drop was from 530 to 379 mm. of water (or 28.4 per cent of the initial pressure). In a third the pressure fell from 460 to 370 mm. of water, a drop of 19.5 per cent. Just how great a reduction in the intra-auricular pressure can be induced without impairment of the peripheral circulation is not yet known, but experience thus far has not suggested that any unfavorable result has been produced.

In one patient, (Case 3), completed catheter studies demonstrate a continuation of the decrease in pressure in the pulmonary circuit after the establishment of the anastomosis (Table I).

The preliminary experiences which make up the substance of the report suggest that at least until some more adequate method is available, the per-

TABLE I.—*Pressure Determinations in Six Patients Operated Upon.*

	Left Intra-Auricular Pressure During Operation (MM. Water)		Pulmonary Artery Pressure (MM. Mercury)			
	Before Anastomosis	After Anastomosis	Resting		After Exercise	
			Pressure	Pulse	Pressure	Pulse
Normal	100 ±	25 ± 0-5	No change
Case 1 O. C. B.	460	N. D.	Before N. D. After N. D.	N. D. N. D.	N. D. N. D.	N. D. N. D.
Case 2 M. Z.	N. D.	N. D.	N. D.	N. D.	N. D.	N. D.
Case 3 R. O.	425	390	46		75	
			Before —	95	—	116
			25		35	
			50		65	
Case 4 D. G.	450	N. D.	After —	78	—	95
			20		25	
			40		104	
			Before —	78	—	100
Case 5 A. P.	530	379	10		40	
			After N. D.	N. D.	N. D.	N. D.
			110		145	
			Before —	95	—	125
Case 6 E. R.	460	370	30		65	
			After Died
			41		65	
			Before —	75	—	98
			18		28	
			After N. D.	N. D.	N. D.	N. D.

N. D.—Examination not done.

formance of an anastomosis between the pulmonary and the systemic venous systems may serve to overcome the effects of excessive pressure in the pulmonary circulation resulting from extreme degrees of stenosis of the mitral valve.

SEVERE MITRAL STENOSIS

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DISCUSSION.—DR. ALFRED BLALOCK, Baltimore: Dr. Sweet is certainly to be congratulated on his excellent results in these extremely ill patients. As he has indicated, surgical attacks have been carried out, experimental and clinical, along several different lines: One, a direct attack on the valve itself; second, a decompressing procedure, such as Dr. Sweet has used; third, a by-passing type of procedure, in an attempt to cause blood to flow from the left auricle to the ventricle, circumventing the valve.

(Slide) The attacks on the valve itself are demonstrated in this slide. In 1922 Drs. Graham and Allen, in this city, attempted to use a cardioscope with a concealed knife in visualizing and in cutting the stenotic mitral valve. Dr. Sweet has referred to the work of Cutler and Beck on the use of the valvulotome as shown in this slide. More recently the late Dr. Horace Smithy used this method with encouraging results.

Dr. Sweet also referred to the work of Harken and of Bailey, in which they make the attack on the commissure itself, rather than on the valve leaflet, attempting to avoid an insufficiency. Harken uses a valvulotome. He has operated on five patients, with two survivals. Bailey uses a curved knife inserted alongside the finger, and attempts to cut the valve at the commissure. He has operated on approximately a dozen patients, with four survivals.

(Slide) Next is the method which Dr. Sweet has used with great success, namely, a decompression procedure. He spoke of the possible use of creating an inter-auricular defect, thereby converting the lesion into a Lutembacher's syndrome.

(Slide) Dr. Hanlon and I have devised what we consider a satisfactory method for creating an inter-auricular defect. It can be done under direct vision. It is dependent upon the fact that the right pulmonary veins are adherent to the posterior wall of the right auricle, and with proper occluding devices one may make an incision into the pulmonary vein, another incision into the auricle, and excise part of the septum.

(Slide) The closure is relatively simple, in that one simply approximates the anterior wall of the auricle to the anterior wall of the vein.

(Slide) Here is an example of such an interauricular defect. We have not attempted to use this in patients with mitral stenosis thus far. We have used it on approximately a dozen patients with transposition of the aorta and the pulmonary artery, and in one patient with a tricuspid atresia.

(Slide) With the dexterity of Dr. Sweet it is perfectly obvious that he can get by with an end-to-end anastomosis between the veins, but anastomoses between veins are particularly apt to thrombose, and I think an inter-auricular defect is somewhat more apt to stay open.

The third and last general method of attack, which I think is still in the experimental stage, is that of a by-passing procedure, first suggested, I think, by Dr. Jeger in Germany in 1913, in which he suggested that one attempt to by-pass the stenotic mitral valve by using a vein graft connecting either the auricle or the pulmonary vein with the left ventricle. I am afraid, however, that the valves in the vein would become incompetent.

More recently Rappaport has suggested the anastomosis of the left auricular appendage to the left ventricle. I am quite confident that this anastomosis will thrombose. I understand that Dr. Robert Gross is now using (at least experimentally) a graft of aorta connecting the auricle and the ventricle.

From a theoretical point of view this method would seem to be the best of all. As to whether the technical features can be worked out, I don't know.

In closing, I would like to urge a vigorous continuation of attempts to produce mitral stenosis satisfactorily in animals. I think the reason this problem has been rather slow in progressing is this difficulty in producing it experimentally. Furthermore, again I would like to congratulate Dr. Sweet on this excellent work.

DR. HENRY SWAN, Denver, Colo.: Gentlemen, I would like to thank you for this privilege of having the floor a moment to discuss this extremely stimulating paper by Dr. Sweet.

We have been interested for some time in investigating both the technical methods and the physiological effects of creating a shunt between the pulmonary and the systemic venous systems. I would like to mention two observations which we have made in regard to this procedure.

(Slide) This slide shows various methods which we have studied in an attempt to make such a shunt. The type of anastomosis which most consistently resulted in a well functioning shunt is illustrated in "D". This is an end-to-end anastomosis between the azygos vein and the upper branch of the pulmonary vein, using a vitallium tube technic. When one does this, of course, one has to ligate the distal end of the vein.

This is followed in our experience by an intense engorgement of the pulmonary tissue, but over a period of about four months this gradually resorbs until the lung tissue returns approximately to normal. In other words, there is no death of the pulmonary tissue, as has been previously reported, and therefore this procedure would be safe if too great an obstruction to the venous return is not made.

(Slide) This slide shows a typical example of a specimen eight weeks after operation, with the probe which has a handle about 4 millimeters in diameter extending from the pulmonary vein to the vena cava.

The second observation is in regard to the physiological effects of such a procedure. As Dr. Sweet pointed out, the purpose underlying the operation is a reduction in the pressure of the pulmonary system by making the shunt from the high pressure area, that is, the pulmonary veins, to a low pressure area—the vena cava. One hopes thereby to prevent or delay the right-sided heart failure.

It must be admitted, however, that in so doing one substitutes a marked increase in the blood flow through the right side for the decrease in pressure.

(Slide) This slide illustrates diagrammatically the situation as it relates to the hemodynamics following such an operation. You will observe that the artificial shunt in this area results in a certain amount of blood, illustrated here as the stippled area, which must continuously pass through the right side of the heart. This can be accomplished only by diminution in the output on the left side of the heart.

Whether in the long run it is better for the right ventricle to have an excessive output against a somewhat diminished pressure, in contrast to a smaller output against a high pressure, only time will be able to tell.

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One final point is in regard to the selection of patients for clinical trial. We are all familiar with the fact that in almost all conditions in which there is a pulmonary hypertension, organic changes occur in the peripheral pulmonary arterioles, quite similar to those which are seen in the systemic arterioles in generalized hypertension.

Such changes are commonly seen in patients with mitral stenosis. If they are present it would seem probable that such a shunt might not result in a lowering of pressure in the pulmonary artery, but indeed might have the opposite effect by increasing the right heart output into a pulmonary bed which is contracted by organic arterial disease.

I would like to ask Dr. Sweet if biopsies were taken on the lungs of any of his patients upon whom he has operated, as this might shed considerable knowledge on this particular point. I should think that if this particular operation were to have its best chance, it would be done early in the course of the disease, before right-sided heart strain has occurred and before there has been any pulmonary arteriolar change.

DR. FREDERICK E. KREDEL, Charleston, S. C.: I should like to say just a word about the problem of insufficiency after valvulotomy.

A little over a year ago Dr. Smithy operated on a series of seven cases of mitral stenosis, with five survivors. In two of these cases the valve was apparently missed, so we cannot count those. One other case subsequently died and did have a little insufficiency, but this was apparently not related to the valvulotomy itself.

In the two other cases, now about one year postoperative, the stenosis has been relieved clinically, and there has been no trouble from mitral insufficiency.

DR. RICHARD H. SWEET, Boston: All of us should be most grateful to Dr. Blalock for his excellent historical review, and to Dr. Swan for his valuable review of the physiologic mechanisms involved in this procedure. I would like also to reiterate the necessity for recreating this condition in animals, and along that line to state that until I had operated on my first patient I was unaware of Dr. Swan's valuable contributions in the experimental animal.

We have not attempted to do this in animals because we, likewise, have failed to create mitral stenosis in any of the experimental animals, and I felt that unless one could reproduce the disease which we are operating upon, there was hardly any wisdom in trying to attempt it on them.

With regard to the choice of patients, of course it is quite obvious that this should not be applied to all cases of mitral stenosis, and I am certain that in fact as we review the cases it will be applicable only to a certain few. Those will be the ones that have hearts that are not enlarged, who have not begun to suffer from the prolonged effects of the disease.

We have done biopsies on the lung. I am not certain about whether I could give any useful information at this point without reviewing the slides regarding the vessels. We were particularly interested in determining, if possible, what it was which made the peculiar appearance in the roentgen-ray films in these patients after recovery from a series of episodes of mitral stenosis. In other words, the lungs of some of these patients looked almost as if they had had miliary tuberculosis, or a certain amount of persistent pulmonary congestion. In fact, that appearance is due to the deposits of hemosiderin which one sees. We will review our slides to see what the vessels look like.

I would like also to point out that this naturally is nothing but a preliminary presentation, and it is a procedure which may ultimately not be of any value; but I am absolutely certain, on the basis of clinical observation, that at least four of these patients are for the moment completely rehabilitated.

THE VALSALVA MANEUVER; AN AID FOR THE CONTRAST VISUALIZATION OF THE AORTA AND GREAT VESSELS*

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RADIOGRAPHIC VISUALIZATION of the vascular system requires a high local concentration of radiopaque dye. In large vessels where the volume flow of blood is great, a sufficient concentration of dye can be achieved by temporary obstruction of the artery proximal to the site of injection. Although this procedure can be carried out with relative ease in the peripheral arteries, it is difficult if not impossible to accomplish this result in the more centrally placed vessels. In retrograde arteriography,^{1, 2} it is particularly difficult to obtain a sufficient concentration of dye, since, as Farinas³ has shown in the experimental animal, the injection, to be successful, must overcome first the inertia of the blood flow and, second, the blood pressure. In a previous study,¹ repeated attempts to visualize the abdominal aorta by retrograde injection of dye into the femoral artery were unsuccessful, in spite of the use of a large needle, 15 or 16 gauge, and the injection of 30 to 40 cc. of 35 or 70 per cent Diodrast. Since proximal compression of the abdominal aorta, especially in its upper portions, was impossible, it was felt that better visualization might be accomplished if some method could be devised for temporary suppression of cardiac output, so that neither the blood pressure nor the volume flow of blood would interfere with the injection of the radiopaque solution.

The Valsalva maneuver was selected as a means for temporary reduction of the cardiac output at the time of the injection of the radiopaque material into the arterial system. The results obtained in a series of 13 cases form the basis for the present communication.

TECHNIC

The following technic has been gradually evolved in the course of these observations, and has been found to be satisfactory in the majority of cases.

The patient is placed supine on a horizontal cassette tunnel; the long axis of the tunnel and the long axis of the roentgen ray table on which it is placed run in the same direction. The tunnel, open at both sides and accommodating a 14 by 17 cassette lengthwise of the table, is put into position in a rack.

This rack has grooves which accept two large lead screens extending from the tunnel in wing-like projections on either side. This is for the protection of

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the films and the operator. On the side of the table away from the operator is a bin, lined with sponge rubber, into which the cassettes fall as they are pushed through the tunnel. The tunnel has a bakelite cover, beneath which are grooves to accept a 14 by 17 Lysholm grid. The channels in the tunnel through which the 14 by 17 cassettes travel have springs at the far end to arrest this travel.

The apparatus is fed by hand, and the exposures are made with a foot switch. Six or seven films are used, and all of the exposures can be made in eight to ten seconds, depending upon the speed of the operator. The interval between the first and second films is usually the closest, due to the fact that one cassette is already in place. The technical factors vary with the vessel to be visualized.

Abdominal Aorta. (1) (Outlined by retrograde carotid injection, using the Valsalva maneuver.) 86 to 92 KV, 0.2 sec., 200 M.A., 36-inch tube film distance. Exposures are made as rapidly as possible beginning just before completion of the injection. (2) (Retrograde injection of the femoral to outline the abdominal aorta and common iliac using the Valsalva maneuver.) Exposures are started at the beginning of injection and are made as rapidly as possible, using the same factors as noted above.

Femoral Artery. 85 KV, 0.15 sec., 200 M.A., 36-inch tube film distance. Exposures are made as rapidly as possible, starting when injection is half completed.

Popliteal and Tibial Vessels. 75 KV, 0.1 sec., 200 M.A., 36-inch tube film distance. Injection is made in the femoral artery. Exposures are made starting with completion of injection. The first two films are exposed one second apart and the later studies made at gradually increasing intervals. Total time for six films is approximately 15 seconds.

Foot and Ankle. 68 KV, 0.05 sec., 200 M.A., 36-inch tube film distance. Injection is made into the femoral artery. Exposures are started at completion of injection. The first two are made within five seconds, and the remainder every five to eight seconds for a total of 30 to 45 seconds.

Thoracic Aorta. (Outlined by retrograde carotid injection using the Valsalva maneuver.) 86 KV, 0.2 sec., 200 M.A., 36-inch tube film distance. Exposures are started at the beginning of injection and made as rapidly as possible.

Forearm and Hand. The method is similar to that in the leg and foot. 60 KV, 0.05 sec., 200 M.A., 36-inch tube film distance. Exposures are started when two-thirds of the injection has been made and they are spaced about every three seconds for a total of 15 to 18 seconds.

The selection of the radiopaque substance is determined by the portion of the vascular system selected for visualization. Thorotrast in a concentration of 20 per cent is non-irritating, and is therefore generally used in the presence of severe obliterative arterial disease or when there is any chance that the contrast medium may enter the intra-cranial blood vessels. Thorium dioxide is not rapidly excreted, and since there may be some damage from persistent

TABLE I

Case No.	Sex	Age	Date	Clinical Diagnosis	Artery Injected	Size Needle	Contrast Medium	Complications	Comments
1.	M	57	6/4/48	Aneurysm abdominal aorta	Rt. superficial femoral	16	40 cc. 70% Diodrast	0	Unsatisfactory. Failure to visualize aneurysm.
2.	M	45	7/7/48	Aneurysm thoracic aorta	Lt. common carotid	16	2 injections 50 cc. 70%	Convulsions; temporary rt. hemiplegia.	Satisfactory with Valsalva maneuver
3.	M	67	1/28/49 2/3/49	Bilateral femoral aneurysms	Lt. carotid Rt. femoral	18 16	30 cc. 70% Diodrast 50 cc. 35% Diodrast	0 0	Satisfactory. Multiple aneurysms of femoral and iliac arteries.
4.	M	48	2/4/49	Thrombosis rt. common iliac artery	Lt. common femoral	16	50 cc. 70% Diodrast	0	Satisfactory. Rt. femoral filled through collaterals.
5.	M	60	2/4/49 2/7/49	Aneurysms bilateral popliteal and abdominal	Rt. femoral Lt. common carotid	16 16	50 cc. 35% Diodrast 2 injections 50 cc. Thorotrast each	0 Dissecting aneurysm aorta. Myocardial infarction.	Unsuccessful. Unsuccessful.
6.	M	69	2/11/49	Bilateral common femoral thromboses	Lt. common carotid	18	40 cc. Thorotrast	0	Satisfactory. Obstruction on left confirmed at operation.
7.	M	50	2/21/49	Thrombosis	Rt. common carotid	18	33 cc. 70% Diodrast	Brain stem damage	Satisfactory. Thrombosis of subclavian, axillary and brachial arteries demonstrated.

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TABLE I.—Continued

Case No.	Sex	Age	Date	Clinical Diagnosis	Artery Injected	Size Needle	Contrast Medium	Complications	Comments
8.	M	49	2/24/49	Aortic thrombosis	Lt. common carotid	16	45 cc. 70% Diodrast	0	Poor aortic filling, but filling of femorals through collaterals.
9.	F	49	3/3/49	Lt. subclavian aneurysm	Lt. brachial	18	25 cc. 35% Diodrast	0	Satisfactory. Arteriosclerotic plaque in subclavian artery; vertebral visualized.
10.	F	67	3/5/49	Polycythemia	Lt. common femoral	18	20 cc. Thorotrast	0	Satisfactory. Multiple occlusions of digital vessels.
11.	M	32	3/18/49	Rt. femoral A-V	Rt. femoral Lt. common femoral	18	30 cc. 35% Diodrast each; 2 injections of left and 1 injection of right femoral	0	Unsuccessful. Failure to show fistula even with Valsalva maneuver.
12.	M	63	3/29/49	Rt. common iliac thrombosis	Lt. common femoral	15	50 cc. 35% Diodrast	0	Satisfactory with Valsalva maneuver
13.	M	25	4/1/49	Post-operative repair of fistulae of rt. popliteal and post. tib. arteries	Rt. posterior tibial	18 Lindemann needle	20 cc. 35% Diodrast	0	Satisfactory; normal arteries.

radio-activity,⁵ its use has been reserved for those patients with degenerative arterial disease whose life expectancy is not great. Thirty-five per cent Diodrast has been found to give less reaction than the 70 per cent Diodrast, and it has been selected for the visualization of the smaller arteries. In those arteries with a large volume flow, for example in retrograde arteriography of the aorta by way of the common carotid arteries, 70 per cent Diodrast has given more satisfactory visualization.

The complications which have resulted from the injection of radiopaque substance during the Valsalva maneuver will be discussed in detail in the consideration of the individual cases.

After the preliminary film has been seen by the radiologist and the surgeon, and any necessary corrections in technic made, the needle is inserted into the artery through the skin or after exposure of the artery under local anesthesia. A number 15, 16 or 18 gauge needle has been used for the femoral and carotid arteries, and for the smaller arteries a No. 18 Lindemann cannula has been found quite satisfactory. This needle is attached to a stop-cock by way of a segment of rubber tubing eight inches long. The rubber tubing is fitted with a "Luer-lok" attachment so that it cannot be detached from the needle. A 50 cc. syringe containing the contrast medium, with a "Luer-lok" connection, is fitted to the stop-cock on the proximal end of the rubber tubing. The use of this section of rubber tubing has been found to be essential in order to prevent dislodgement of the needle from the artery during the forceful injection. While the operator holds the needle in the lumen of the vessel, the assistant grasps the barrel of the syringe in one hand and the plunger in the other hand, in preparation for the injection. The patient is then instructed to take a deep breath, to close the glottis, and to strain down with all his might. If the artery has been exposed, the decline in blood pressure is readily perceptible to the index finger of the surgeon who is holding the needle in the arterial lumen. When the injection is being made directly through the skin, the disappearance of the pulse at the wrist or at the temple during the forced expiration against resistance serves as a guide for the injection of the contrast material.

When the blood pressure has fallen to a low level, the signal is given and the radiopaque solution is injected as rapidly as possible. Although the exact time of the injection has not been measured, it has been estimated that from two to five seconds is required for the injection of 30 to 50 cc. of solution. The first film is exposed when about half of the contrast material has been injected, and thereafter the succeeding films are exposed every two to five seconds, depending upon the portion of the arterial system which has been selected for visualization. In the aorta and its major branches the cassettes are changed as rapidly as possible, every one to two seconds, while in the most peripheral arteries in the distal parts of the extremities longer intervals have been found more satisfactory. In patients with a high degree of arterial tone, it may be advisable to precede the visualization by injection of Procaine into the region of the sympathetic ganglia.

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It is advisable to have the patient practice the Valsalva maneuver several times before the injection in order to familiarize himself with the details. Again, the patient should be warned that he will experience a sensation of intense heat at the time of the injection, and that this painful sensation is of a temporary nature, but that he should refrain from any movement while the exposures are being made. If Diodrast is being used, preliminary tests for sensitivity, of course, are necessary.

RESULTS

The effect of forceful expiration against the closed glottis, the Valsalva maneuver, upon the blood pressure, is illustrated in Figure 2. There is a rapid

FIG. 1

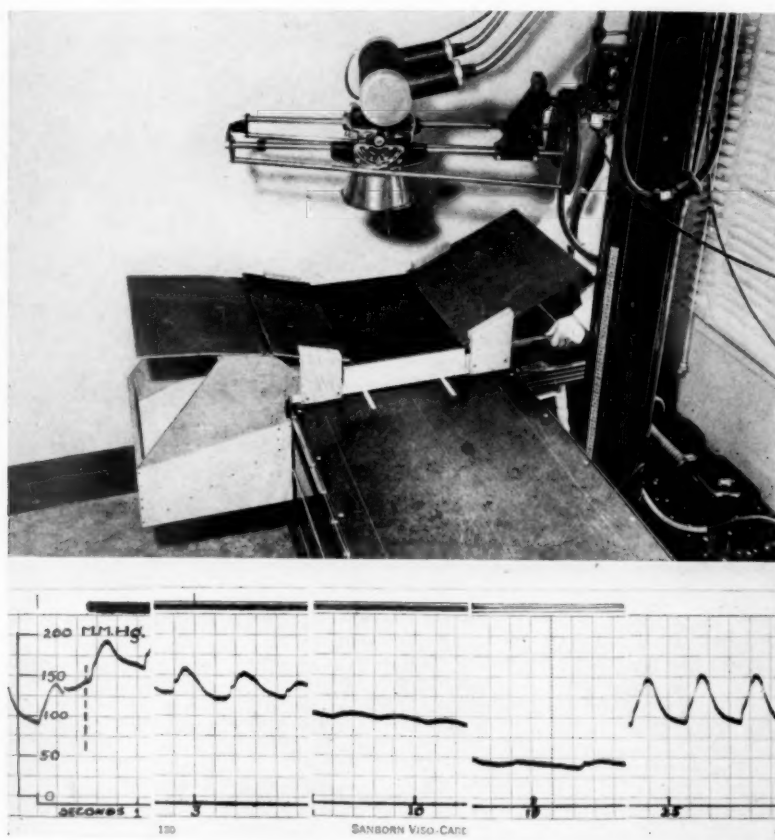


FIG. 2

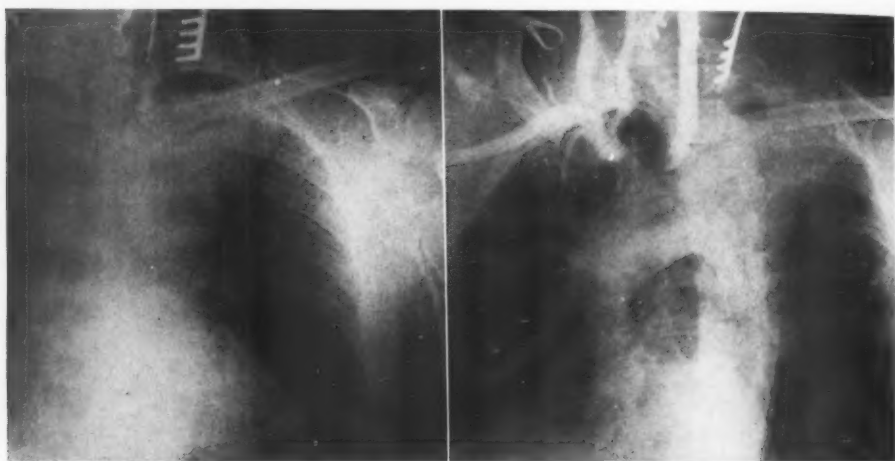
FIG. 1.—Rapid film changer. Exposure made by foot switch; films fall into bin as completed.

FIG. 2.—Arterial pressure tracing. Strain gauge recording of femoral blood pressure variations during a Valsalva maneuver. Dotted line shows point of commencement of expiration effort following maximal inhalation. Note drop in total pressure and pulse wave during 20-second interval of expiratory effort against a closed glottis. The last frame indicates the temporary overshoot of pressure following release.

decline in the blood pressure and pulse amplitude over a period of 20 seconds; in this particular subject the blood pressure as recorded by a strain gauge fell to 48 mm. of mercury. Following release of the glottis, the blood pressure rapidly rises and usually exceeds the initial level.⁴

The first retrograde arteriogram with the use of the Valsalva maneuver was performed in the following patient:

Case 1.—This patient, a man of 57, was admitted to the Franklin Hospital in June of 1948, with the chief complaint of intermittent attacks of abdominal pain of a year's duration. One year before admission he had been struck by a heavy case in the mid-abdomen, and subsequently had experienced attacks of abdominal pain radiating into both flanks. His physician had noted a pulsating abdominal mass, and roentgenogram of the abdomen had revealed a circular calcified shadow lying at the level of the fourth vertebra,



A

B

FIG. 3. (Case 2)—Retrograde left common carotid arteriogram. (A.) Aneurysm of arch of aorta is faintly visualized. (B.) Clearer delineation of the same lesion with Valsalva maneuver and visualization of the ascending aorta.

which had been interpreted as an aneurysm of the abdominal aorta. Retrograde arteriography of the abdominal aorta was performed by the injection of 41 ccs. of 70 per cent Diodrast through a 16-gauge needle. With a special apparatus, the injection was made at a pressure of 100 lbs. per square inch over a period of 3 seconds, and 2 films were exposed. The radiopaque material rose as high as the second lumbar vertebra, and by-passed the calcification seen on the left side of the vertebral column. As a result of this study, it was concluded that the calcified mass did not appear to be an aneurysm, since it lay outside of the aorta.

Exploration through a retroperitoneal exposure was performed on June 11. The mass proved to be an aneurysm of the abdominal aorta which had apparently expanded on numerous occasions with resulting marked inflammatory scar tissue. After preliminary occlusion of the aorta above and below the aneurysm, the mass was opened, but surgical repair was found to be impossible because of marked sclerotic changes in the wall of the aorta, where a defect measuring one inch in length and involving one-third of the anterior wall was found. The aorta was completely divided above the sac, and the opening closed with a running suture of No. 40 cotton. After operation, in spite of the use of anticoagulant and supportive measures, there was marked ischemia of the lower half of the body leading to the patient's death on the second postoperative day.

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Comment. Postmortem examination showed extensive degenerative arterial disease involving the aorta and iliac vessels. This was the first patient in whom the Valsalva maneuver was used for retrograde arteriography of the abdominal aorta, and although the roentgen ray films were better than any previously obtained, they still were not sufficiently clear to demonstrate the extensive arterial disease present and the communication of the aorta with the aneurysmal sac.

Case 2.—This patient was a 45-year-old man, who was admitted to the Franklin Hospital in July of 1948 for an attempt at visualization of an aneurysm involving the transverse aortic arch. The patient had suffered massive hemoptysis in January, 1948, and at that time the diagnosis of a luetic aneurysm of the aorta was made. Retrograde arteriography using the left common carotid artery was performed on July 7, 1948. Under local anesthesia the left common carotid artery was exposed, and through a 16-gauge needle 50 cc. of 70 per cent Diodrast were injected, with the patient in the dorsal recumbent position. The patient experienced some discomfort and nausea. He was then rotated into the left anterior oblique position, and the injection repeated, but this time using the Valsalva maneuver. The Diodrast was injected when the pressure in the carotid artery had dropped to a low level. In Fig. 3 is shown a comparison of the intensity of visualization of the aorta and its large branches, with and without the Valsalva maneuver.

Twenty seconds after the injection of the Diodrast, the patient had a generalized convulsion which lasted for 30 seconds and was followed by a prolonged period of apnea with a slow and irregular pulse. When spontaneous respiration was finally resumed the patient was given nasal oxygen. After completion of the procedure, it was found that the patient had a right hemiplegia. He remained comatose for one-half hour and the convulsions recurred on three occasions. He was treated with nicotinic acid, 100 mg. every four hours, and nasal oxygen; after a severe convulsion when the heart appeared to have stopped, he was given intracardiac adrenalin. Recovery finally took place without residual neurological symptoms, but the hemoptysis has recurred.

Comment. The convulsions and temporary right hemiplegia in this case were probably due to an error in technic which allowed the 70 per cent Diodrast to reach the intracranial circulation in a concentrated form. As emphasized previously,² it is extremely important to aspirate the 70 per cent Diodrast from the left carotid artery after completion of the injection, and it is possible this was not done in this patient. Again, it is possible that the 70 per cent Diodrast might have entered the intracranial circulation by the right carotid and by both vertebrals (as shown in Figure 3B). In retrospect it would have been better to have used Thorotrast for this visualization.

Case 3.—This patient was a 57-year-old man who was admitted to the Franklin Hospital in January of 1949 because of a pulsating mass in his right groin. His blood pressure was 230/150. On physical examination a pulsating mass was found in both inguinal regions. There was evidence of mild cardiac decompensation.

Retrograde carotid arteriography, using 30 cc. of 70 per cent Diodrast through an 18-gauge needle, was attempted, but because of the patient's poor general condition, the Valsalva maneuver was carried out with caution and only mildly, and the dye was not injected with as great force as usual. In serial films of the abdomen no dye was visible in the abdominal aorta below the level of the renal artery. The patient recovered from this procedure without complications.

On February 3, a retrograde arteriogram of the right femoral artery was obtained by insertion of a 16-gauge needle directly through the skin into the femoral artery just below the aneurysm in the inguinal region. The circulation below the point of insertion of the needle was temporarily obstructed by inflation of a tourniquet applied to the thigh and 50 cc. of 35 per cent Diodrast were injected. As shown in Fig. 4, multiple saccular aneurysms of the right iliac artery were disclosed as well as a large fusiform aneurysm of the right external iliac and femoral arteries.

In view of the patient's generalized cardiovascular disease, operative treatment did not appear to be indicated.

Case 4.—This patient was a 48-year-old man who was admitted to the Franklin Hospital in February of 1949 because of intermittent claudication involving the right thigh and leg of six months' duration. Although the left femoral pulse was readily palpable, no pulse could be felt in the right groin. The pulsation of the abdominal aorta appeared to be normal.

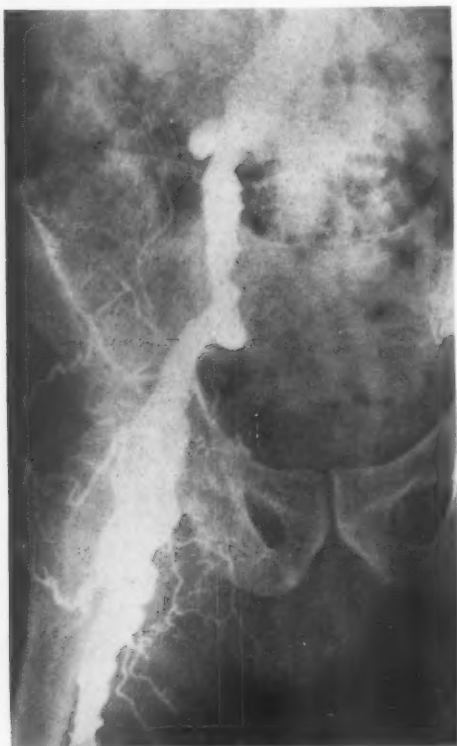


FIG. 4. (Case 3)—Retrograde right femoral arteriogram. Aneurysms of femoral and iliac arteries are demonstrated.

Under local anesthesia the left femoral artery was exposed in the groin, and 50 cc. of 70 per cent Diodrast were injected through a 16-gauge needle over a period of four seconds while the circulation to the left-lower extremity was occluded by inflating a tourniquet placed about the thigh. Serial films were taken which showed obliteration of the iliac artery on the right side, with filling of the right femoral by means of collaterals across the pelvis from the left side.

Comment. This patient was allowed to exhale before completion of the injection, so that filling of the abdominal aorta was not obtained. Even though the radial pulse disappears more completely immediately following release of the breath, it is apparently advisable to maintain the increased intrathoracic pressure during the entire period in which films are being taken.

Case 5.—This patient was a 60-year-old man who was admitted to the University of California Hospital in January of 1949 because of a pulsating mass behind the left knee. In July of 1948 he had suddenly noted pain and numbness, with

pallor and coldness of the left lower leg, but recovery had taken place. At the time of admission, he had a blood pressure of 210/130, his heart was enlarged, and a pulsating mass was palpable in the lower abdomen. In addition, there was dilatation of the left popliteal artery. Retrograde arteriography by way of the right femoral was attempted on February 4, but was unsatisfactory due to the fact that the patient moved during the exposure of the films. The patient's movement was probably due to the intense burning sensation from the injection of 35 per cent Diodrast.

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Retrograde carotid arteriography with the Valsalva maneuver was attempted on February 7, using Thorotrast. Two injections of 50 cc. each of 20 per cent Thorotrast by way of the left common carotid artery were made. In spite of the use of the Valsalva maneuver, no dye appeared in the lower abdominal aorta or pelvis. It was the opinion of Dr. Earl R. Miller, of the Department of Radiology at the University of California Hospital, that some additional vascular lesion must have been present in the thorax to prevent the passage of radiopaque material into the abdomen.

At the time of the second injection of Thorotrast, the patient experienced a sensation of pressure in the thorax, but no significant pain. That night, some eight hours later, he had a sudden onset of severe precordial distress, with a fall in blood pressure, and other

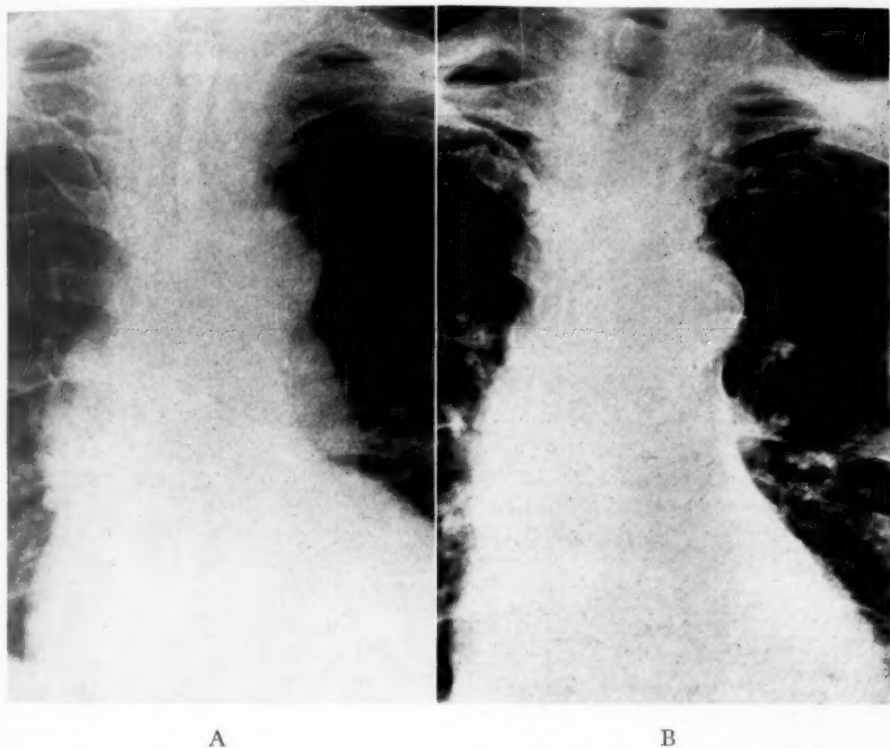


FIG. 5. (Case 5)—Roentgenogram of chest. (A.) Preoperative film. (B.) Film ten days after retrograde carotid arteriogram, showing residual Thorotrast in wall of aorta.

classical signs of acute myocardial infarction. The electrocardiogram showed typical changes, and there was an elevated sedimentation rate and fever with persistent chest pain for a period of 10 days. At the end of that time, however, a roentgenogram of the chest showed radiopaque material present within the wall of a dilated aorta as shown in Fig. 5. Recovery finally took place.

Comment. This patient probably had an unsuspected dissecting aneurysm of the thoracic aorta. During the period of hypotension from the Valsalva maneuver he might have sustained a coronary occlusion or else, possibly during the period of hypertension following release of the glottis, a further rupture of a dissecting aneurysm took place.

Case 6.—This patient, a 69-year-old man, was admitted to Franklin Hospital in February of 1949 because of a dull aching pain in both feet and lower legs which had been present over a year. On admission he complained of a constant pain in the region of his left ankle and in the metatarsal area. The left common carotid artery was exposed and 40 cc. of Thorotrast were injected in a retrograde fashion through an 18-gauge needle at the height of a Valsalva maneuver. The entire injection required about 4 seconds. Serial roentgen-rays were taken immediately following the completion of the injection. These films demonstrated occlusion of the common femoral arteries bilaterally, which was confirmed on the left by operation. The occlusion on the left was probably acute with ischemic neuritis, while that on the right was of a more chronic nature. Temporary relief was obtained by left femoral arterectomy. Following recurrence of pain,

FIG. 6



FIG. 7

FIG. 6. (Case 7)—Retrograde carotid arteriogram with Valsalva maneuver. Serial films show obliterated subclavian, axillary and brachial arteries.

FIG. 7. (Case 9)—Retrograde left brachial arteriogram. (A.) Arteriogram without use of Valsalva maneuver demonstrating filling to the junction of the axillary and brachial arteries. (B.) Same procedure with Valsalva maneuver demonstrating filling of the subclavian to its origin as well as of the vertebral. Note the narrowing of the subclavian artery at the origin of the vertebral.

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relief was obtained by left lumbar sympathectomy after left lumbar sympathetic block had proved effective.

Comment. The retrograde arteriogram was useful in showing where the obstruction lay, so that a successful arterectomy could be carried out.

Case 7.—This patient, a man of 50, was admitted to the Franklin Hospital in February of 1949 because of burning pain, numbness, and paralysis of the right arm and hand of four months' duration. This state followed excision of a small tumor from the right axilla. The skin of the hand was glossy and cool; the joints were fusiform and fixed. Pulses were absent in the right wrist; however, the brachial was palpable at the elbow. The problem here was one of locating the point of arterial obstruction, of determining its extent, and its relation to the causalgic state.

Under local anesthesia the right common carotid artery was exposed and 35 cc. of 70 per cent Diodrast were injected in a retrograde fashion at the height of a Valsalva maneuver. Films were exposed serially, the first being taken when half of the radiopaque material had been injected. This demonstrated obliteration of the subclavian, axillary and brachial arteries from the second portion of the subclavian to beyond the profunda brachii. The rapid injection of Diodrast combined with arterial obstruction and the Valsalva maneuver caused the medium to fill the internal mammary and vertebral arteries in high concentration. A posterior inferior cerebellar syndrome resulted from the concentrated Diodrast in the vertebral artery, from which recovery was gradual over a period of 3 weeks.

Comment. Excellent visualization was obtained facilitating arterectomy in combination with sympathectomy and brachial plexus neurolysis to relieve this patient's painful syndrome. The use of 35 per cent Diodrast and concomitant occlusion of the vertebral artery probably would have avoided the brain stem injury.

Case 8.—This patient was a 49-year-old man who was admitted to Franklin Hospital in February of 1949 because of a 3-year history of claudication in both hips. There was definite evidence of an arterial insufficiency in both lower extremities. The femoral pulses were palpable but that on the right was diminished. There were no palpable arterial pulsations distal to the femoral region. The left common carotid artery was exposed, a 16-gauge needle was introduced in a retrograde fashion, and 45 cc. of 70 per cent Diodrast were injected into the left common carotid artery. The injection was carried out during a Valsalva maneuver, and roentgen-ray films were taken serially. The aorta and iliac arteries were shown to be very faintly outlined; the dye was seen entering the femoral artery, and the femoral profunda was well outlined.

Comment. These films show poor aortic filling but good filling of the femorals by collaterals. The poor visualization was due to a combination of an inadequate Valsalva maneuver (limited because of the patient's condition), slow injection, and insufficient Diodrast.

Case 9.—This patient was a 49-year-old woman physician, admitted to the Franklin Hospital in March of 1949 because of one year's history of numbness and paresthesia of the third, fourth and fifth fingers of the right hand. On examination all pulses were present, both in the upper and lower extremities. Feet and hands were moist, showing marked evidence of vasoconstriction. While being investigated for a scalenus syndrome, a systolic murmur was found over the left subclavian artery which was transmitted into the left axilla, and, being a physician, the patient was worried that she might have an aneurysm.

Under local anesthesia, the brachial artery was exposed in the mid-arm, and an 18-

gauge needle was introduced in a retrograde fashion into the vessel. With distal occlusion, 25 cc. of 35 per cent Diodrast were injected rapidly into this vessel and serial films taken. These films showed no filling proximal to the junction of the axillary and brachial arteries. (Fig. 7A)

The same procedure was carried out a second time, this time with the Valsalva maneuver, and revealed filling at the origin of the subclavian artery and also demonstrated a small notch in this vessel immediately distal to the origin of the vertebral artery. The opaque material entered the vertebral artery and was traceable to the base of the skull. (Fig. 7B)

Comment. Here retrograde arteriography was useful in showing that there was no aneurysm present.

Case 10.—This 67-year-old woman was admitted to the Franklin Hospital because of the development of small circumscribed areas of induration with inflammation in the skin of her toes. In March of 1949 a left femoral arteriogram was performed with an 18-gauge needle, 20 cc. of Thorotrast being injected at the height of a Valsalva maneuver. Occlusion of digital vessels was demonstrated. (Fig. 8)



FIG. 8. (Case 10)—Femoral arteriogram with Valsalva maneuver showing clear delineation of digital vessels. Note multiple areas of arterial obliteration.

Comment. The use of the Valsalva technic made possible a sufficient concentration of Thorotrast in the smaller vessels so that the digital vessels could actually be visualized.

Case 11.—This 32-year-old man was shot in the right upper thigh in December of 1948. Two weeks after his injury the patient was observed to have a systolic bruit and thrill over the right femoral vessel just below the inguinal ligament. Proximal occlusion of the femoral vessel caused a pulse decrease of 90 beats to 67 beats per minute.

An unsuccessful attempt to visualize the right femoral vessel was made by retrograde arteriography from the left common femoral. The right common femoral was then injected in a retrograde fashion with 30 cc. of 35 per cent Diodrast, through an 18-gauge needle. Serial roentgenograms were taken beginning when the injection was half completed, and demonstrated an aneurysmal dilatation of the common femoral artery almost at the site of the arterial puncture which filled very poorly.

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FIG. 9

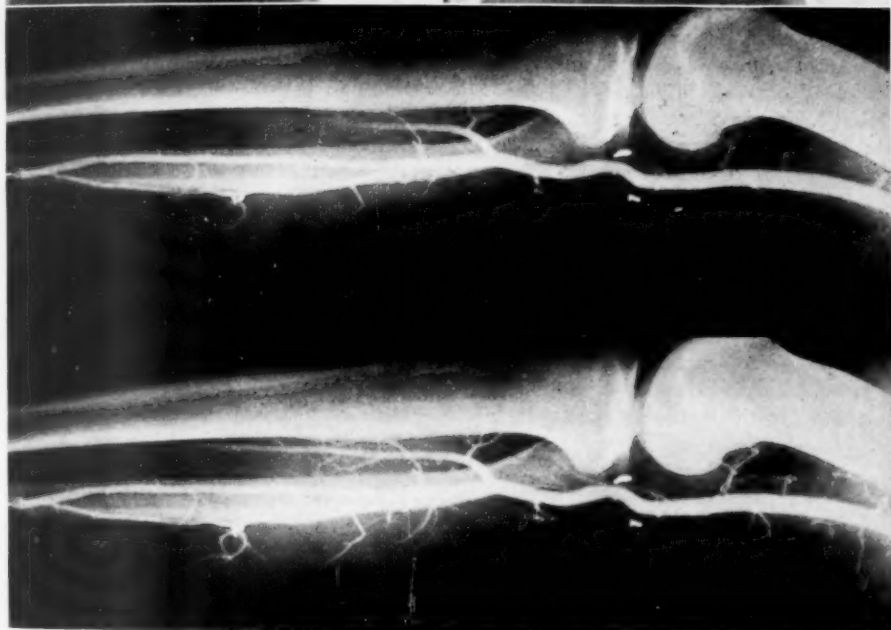
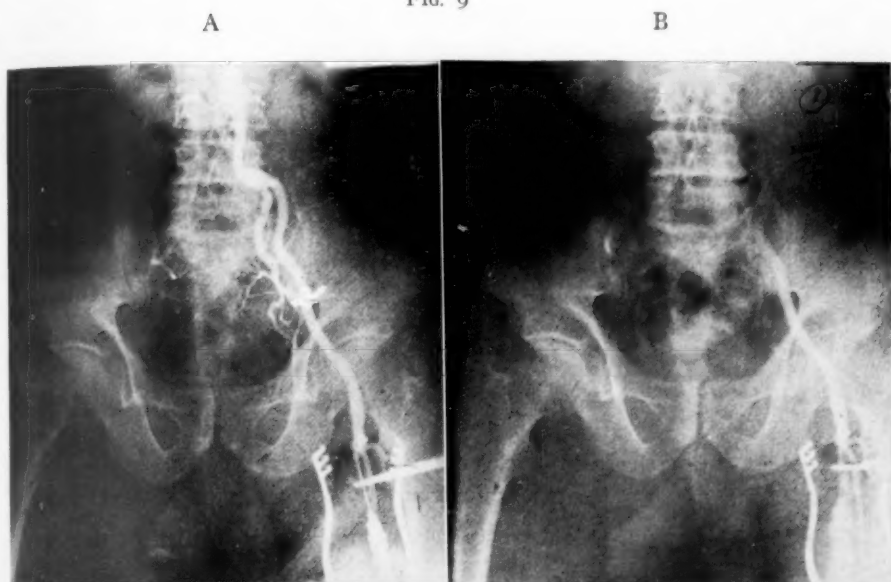


FIG. 10

FIG. 9. (Case 12)—Left retrograde femoral arteriograms performed with (A) and without (B) Valsalva maneuver. Note in (A) the filling of the abdominal aorta and the crater at the origin of the right common iliac artery, which is obliterated.

FIG. 10. (Case 13)—Right retrograde posterior tibial arteriogram with Valsalva maneuver.

Comment. This is the first case in which we were unable to demonstrate an arterio-venous fistula, and retrograde carotid arteriography probably should have been performed. Surgery demonstrated two arterio-venous aneurysms.

Case 12.—This 63-year-old man was admitted to Franklin Hospital in March of 1949 because of intermittent claudication in his right leg and thigh of one year's duration. Physical examination showed a faint right femoral pulse but no pulsations distal to this point. The arterial pulsations of the left lower extremity were normal. The left common femoral artery was exposed surgically. Through a 15-gauge needle 50 cc. of preheated 35 per cent Diodrast were injected in a retrograde fashion, after the blood pressure had been reduced to a low level by a Valsalva maneuver. Serial films were taken beginning when about 35 cc. of the Diodrast had been injected. The same procedure was then repeated without the Valsalva maneuver. Each injection required 3 to 4 seconds for completion. In the films taken during the Valsalva maneuver, the Diodrast was seen at the level of the renal artery. The films demonstrated a filling defect with a crater in the right common iliac artery with obliteration of the lumen for $1\frac{1}{2}$ inches. (Fig. 9)

Comment. The arteriogram was helpful in this case in locating the area of obliteration, and right lumbar sympathectomy has given marked relief.

Case 13.—This 25-year-old veteran was admitted to Franklin Hospital for circulatory study in the Veterans Administration Vascular Research Project as set up by the Subcommittee on Vascular Surgery of the National Research Council. This patient had sustained a shrapnel wound resulting in two arterio-venous aneurysms, one of the right popliteal artery and one of the posterior tibial artery and vein. These were repaired by the senior author (N. E. F.). The pulses were present in both extremities; however, the pulses in the right foot were diminished in comparison to those of the left. Arteriography had previously been attempted in an army hospital, resulting in extravasation of Thorotrast into the femoral area and subsequent development of an indurated mass in the femoral triangle. For this reason retrograde arteriography was selected.

The posterior tibial artery was exposed two inches above the medial malleolus. Inasmuch as an ordinary sharp-bevelled needle was found to lacerate the wall of the small vessel, making pressure injection difficult, a round Lindemann cannula was used. This technic may be advisable in injecting small arteries. A Valsalva maneuver was initiated and at its height 20 cc. of 35 per cent Diodrast were injected in a retrograde fashion, and serial films were taken, the first film being taken when the Diodrast had been half injected. Following this procedure the posterior tibial pulses could be felt distal to the point of injection. In this patient a completely normal popliteal and posterior tibial artery were demonstrated following reconstructive endo-aneurysmorrhaphy. (Fig. 10)

Comment. In this patient it is demonstrated that it is possible to visualize the main arterial channels of the leg and thigh by retrograde injection. It is interesting to note the persistence of collaterals five years after repair of an arterio-venous fistula.

DISCUSSION

In the year 1740 there was published in Venice a treatise written in Latin: "*The Works of That Most Celebrated Man, Antonio Valsalva, That Is, His Tract on the Human Ear and His Anatomical Dissertations.*" Through the kindness of Professor J. B. deC. M. Saunders of the Department of Anatomy, University of California Medical School, the following translation has been made from Valsalva's observations on the physio-pathology of suppuration in the middle ear:

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"I say that if by closure of the mouth and nose the air contained within is compressed, then pus may be freely extruded by this act. . . ."

The Valsalva maneuver has been used in physiological experiments, both in the experimental animal and in human subjects, as a means of altering cardiovascular hemodynamics. Bruck⁶ conducted extensive studies on the cardiovascular changes produced, and refers to the Valsalva maneuver as a well-known physiological phenomenon. Wiggers⁷ has discussed the mechanism of the changes in pulse and blood pressure and in 1923 published a pulse tracing, taken with optical recording, of the alterations which took place when the intrathoracic pressure was suddenly increased. This maneuver has been used extensively by Wilkins and his collaborators^{4, 8} as a means of evaluating the sympathetic innervation in patients with hypertension. The period of forced expiration was limited to ten seconds in their cases, and chief interest was focused upon the rise in blood pressure following release of the glottis.

In the series of patients here reported the Valsalva maneuver was used chiefly to depress the cardiac output. If the intrathoracic pressure is increased for a longer period than ten seconds, almost complete suppression of the pulse can be obtained in the majority of cases, and as shown in Fig. 2, the blood pressure can be reduced to low levels. It is probably significant that the only case in this series in which it was impossible to visualize the arterial system successfully with the use of the Valsalva maneuver was Case 11. This patient had a large arterio-venous fistula, involving the right femoral artery and vein. The failure of the Valsalva maneuver to allow retrograde flow of the radiopaque material may have been due in this case to the fact that the large communication between arterial and venous systems resulted in such a rapid filling of the right side of the heart that it was impossible to reduce the cardiac output by means of increasing the intrathoracic pressure.

The Valsalva maneuver is not without danger, especially in patients with degenerative cardiovascular disease. During the period of hypotension resulting from the reduced cardiac output, there may be sufficient anoxia, both of the myocardium and of the brain, to produce irreversible changes, or even to produce intravascular thrombosis. It is possible that in Case 5, the coronary occlusion which developed a few hours after this procedure may have been due to the lowered blood pressure associated with the Valsalva maneuver. On the other hand, in patients with pre-existing hypertension, as Wilkins has shown,⁴ the hypertension following release of the forceful expiration may be sufficient to cause the rupture of some weakened segment of the arterial tree. The demonstration of radiopaque material within the walls of the dilated thoracic aorta in Case 5 can only have been due to a rupture of the intima of the aorta at the time that the radiopaque material was within the lumen.

A third possible danger in the use of the Valsalva maneuver arises from the fact that the concentration of radiopaque material within the vascular system is greater than without the use of this procedure. Special precautions should therefore be taken to prevent this material in concentrated form from reaching portions of the vascular system where it may produce injury. In Case 2 and

in Case 7, it is probable that the complications which developed resulted from the high concentration of 70 per cent Diodrast in the intracranial arteries. Although we have encountered no instances in which myocardial injury was produced by the entrance of 70 per cent Diodrast into the coronary arteries, it seems possible that with the injection of 70 per cent Diodrast in a retrograde fashion into the right or left common carotid artery, a sufficient concentration of the dye could be present in the aorta to allow some of the 70 per cent Diodrast to enter the coronary circulation.

Arteriography is not a harmless procedure, and it is our opinion that it should be used only in those cases in which the visualization of the vascular system can contribute to a better understanding of the pathological process and to the treatment, medical or surgical, in the individual case.

SUMMARY

Radiographic visualization of the vascular system requires a high local concentration of radiopaque dye. In large vessels where the volume flow of blood is great, the injected dye is rapidly diluted and visualization is difficult. Temporary diminution of the cardiac output by means of the Valsalva maneuver (forced expiratory effort against the closed glottis) permits injection of radiopaque material into a major vessel containing relatively stagnant blood. With subsequent return of blood velocity, which occurs when the patient exhales, this material traverses the arterial system as a bolus in sufficient concentration to be visualized in successive roentgen ray films. This technic has been used in 13 patients, by both direct and retrograde arteriography for visualization of the thoracic and abdominal aorta, as well as of the major peripheral arteries. Satisfactory visualization was obtained in ten of the 13 cases. The dangers of the successive hypotension and hypertension produced by this maneuver are emphasized.

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THE VALSALVA MANEUVER

DISCUSSION.—DR. REGINALD H. SMITHWICK, Boston: I have not had any experience with the Valsalva maneuver in arteriography, but Dr. Wilkins and I have been very much interested in it as a means of studying reflex control of blood pressure in normotensive and hypertensive patients.

I would like to show one slide because I think it will illustrate very clearly the hemodynamics that are concerned in this maneuver which Dr. Freeman has taken advantage of in arteriography.

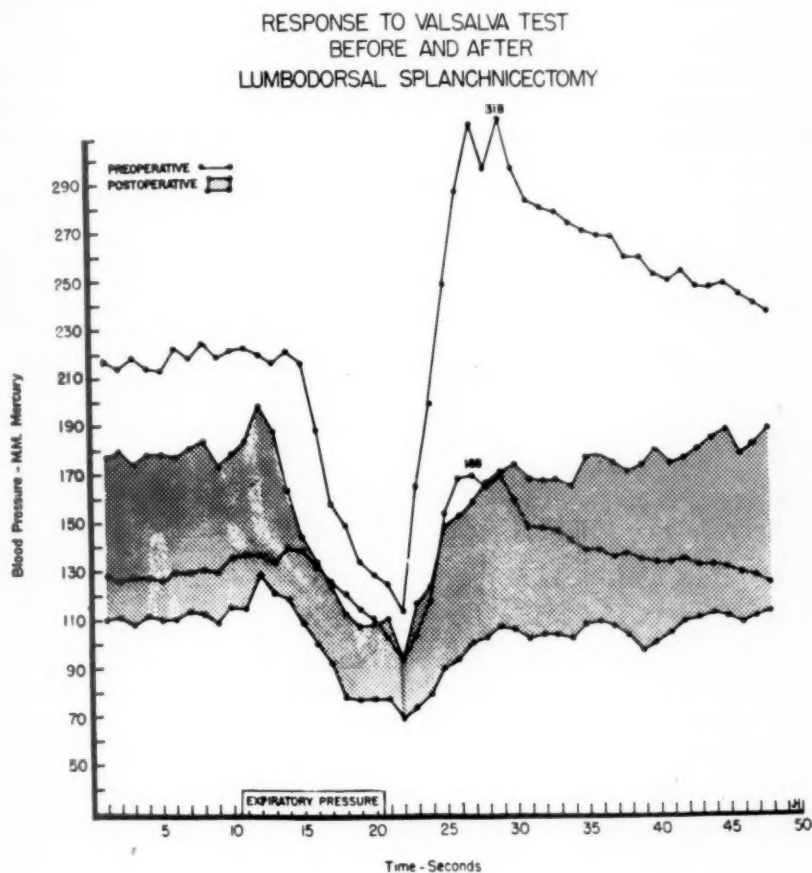


FIG. 1

In our studies we have made continuous records of blood pressure by means of intra-arterial recordings with a Hamilton manometer. The above figure is an illustration of a Valsalva maneuver as we carry it out in the study of hypertension. The solid line is the preoperative observation, and the shaded chart indicates the effect of a thoracolumbar splanchnicectomy upon blood pressure.

During the ten-second period of forced expiration against a positive pressure of 40 millimeters of mercury, as Dr. Freeman has indicated, the blood pressure falls precipitously, as shown here, because of decreased venous return and cardiac output.

When the expiratory period ceases the blood pressure falls for one pulse beat after the period of expiration, and then during the succeeding five pulse beats over a period

of about five seconds there is this extraordinary overshoot of blood pressure to very high levels. In this case it went to 318/168. It shows that this maneuver can result in tremendous overshoots of blood pressure, and may be hazardous.

Following the denervation of a large vascular area, as shown by the tracing, the blood pressure falls in a similar fashion during the Valsalva maneuver, but after that there is a very much less precipitous rise in pressure, which in thoroughly denervated patients gradually comes up to the previous base line but never overshoots it. This we regard as one of the very important physiological effects of extensive sympathectomy and believe it to be of considerable therapeutic value in the management of hypertension.

I might say that these same sort of responses may be seen in patients with coarctation of the aorta, and they may have marked overshoots as judged by the Valsalva maneuver, as many hypertensive patients do. That, incidentally, is the rationale for our having operated upon a series of patients with coarctation of the aorta that are beginning to get into difficulty in the older age group. We hope that by modifying these reflex variations in blood pressure, the progress of cardiovascular disease will be slowed. So far, the patients seem to have done very well, although we have only a small series and some cases have been observed for only a short period of time.

The abolition of the sharp overshoot following the Valsalva maneuver can also be accomplished by means of sympatholytic drugs. I mention that simply because it might be that if this period is hazardous in arteriography, the use of a short-acting sympatholytic agent given prior to the maneuver might eliminate some of the complications Dr. Freeman has mentioned. It might also not in any way interfere with the success of the arteriography, and, because of the slower rise in blood pressure, might give a longer period of time to expose the films.

DR. NORMAN E. FREEMAN, San Francisco: I want to thank Dr. Smithwick for his very valuable suggestion. I believe his suggestion of the use of some sympatholytic drug to prevent the marked overshoot is an excellent one.

In general, I have emphasized the hazards of this maneuver because of the fact that it is dangerous procedure, and that we hesitate to employ it, especially in the older age group. I feel, however, that in some cases it is the only way in which an effective arteriogram which will determine therapy can be obtained.

Of the total number of cases in which this maneuver was used—I think there were about 17 cases—I have emphasized the three complications we have had, two in which the dye reached the intracranial circulation, and one who had an extravasation of the dye into the walls of the aorta. The other 14 cases showed no undesirable side effects.

In general, I think it is advisable to expose the artery, since this material is injected very rapidly by an assistant, and it is wise to have the needle connected to the syringe by means of a short section of rubber tubing to prevent the needle from being dislodged by the forceful injection.

SURGICAL TREATMENT OF INSIDIOUS THROMBOSIS OF THE AORTA*

REPORT OF TEN CASES

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THROMBOSIS OF THE AORTA, insidious in nature, and not the result of so-called saddle embolus, is a disease rarely observed and reported. In the last 20 months, ten patients have been seen with this condition. Although reports in the literature of *embolic* obliteration of the bifurcation are numerous, those of *thrombotic* of the terminal aorta are noticeably few. Little effort has been made to differentiate between the two entities despite the fact that both were described as early as 1814 by Graham.¹

A case reported by Barth² in 1848 is one of the first in which *insidious obliteration* of the aorta was considered. In this patient, a cylindrical thrombus developed and extended from the superior mesenteric artery to the aortic bifurcation, leaving a narrow channel for the flow of blood. The author observed that no circulatory changes were manifest at onset, but numbness in the lower extremities and intermittent claudication became apparent at a later date.

In most instances, reports have been made of groups of patients with embolism, with or without secondary thrombosis, in addition to those having primary thrombosis of the aorta. In 1898, Welch³ collected all the reported cases of thrombosis and embolism of the terminal aorta. In this group of 59, 14 were considered to be thrombotic, and of these, seven were primarily thrombotic. In 1923 this lesion was again reported by Leriche.⁴ In 1940, he described the symptom complex and diagnostic criteria, and reported five cases in which the diagnosis was clearly substantiated at operation.⁵

In 1943, Greenfield⁶ reported 156 cases of thrombosis and embolism of the abdominal aorta, including five of his own, and the group previously reviewed by Welch. No clinical differentiation was made between the two conditions. Holden (1946)⁷ reported two cases of thrombotic occlusion of the aorta treated by sympathectomy with good results. Recently (1948), Leriche⁸ published a classic description of the syndrome of obliteration of the terminal aorta by thrombosis and its differentiation from occlusion by an embolus.

ETIOLOGY AND PATHOLOGY

The bifurcation of the aorta is the site at which atheromata are most likely to develop, and at which arteriosclerosis is intensified, often with the production of ragged, calcified, ulcer-like areas in the intima. Thus it is a susceptible point for the formation of a thrombus with ultimate narrowing

* Read before the American Surgical Association, St. Louis, Mo., April 20, 1949.

and constriction of the lumen. Gross and Philips⁹ in 1940 pointed out that thrombosis of the abdominal aorta may occur in the presence of an ulcerated arteriosclerotic plaque, a dissecting aneurysm, arteritis, or congenital narrowing of the aorta. Why it is not a more common observation at autopsy in patients with severe arteriosclerosis at this site is not known.

As Leriche⁸ has pointed out, the thrombosis may be progressive in that it frequently arises in the iliac arteries and propagates upward to eventually obliterate the aortic lumen at the bifurcation and just above that point. Death frequently results from hypertensive cardiovascular disease and uremia which follows the progression of the thrombus up to and above the origin of the renal arteries.



FIG. 1, Case 2.—Resected bifurcation of the aorta showing thrombus.

Examination of the excised bifurcation of the aorta in one of the cases reported here revealed findings typical of this disease (Fig. 1). The specimen consisted of a segment of the aorta and common iliac arteries, 5 cm. long, occluded by a thrombus. There was calcification in the wall of the aorta and in the thrombus. Microscopic examination showed marked intimal proliferation in both the aorta and the iliac artery. There were large calcified plaques between the media and the intima with areas of degeneration of the media.

SYMPTOMATOLOGY

The predominant symptoms in the patients observed were pain in the hips and legs, easy fatigability, and intermittent claudication in the lower extremities (Table I).

Next to pain, the most pronounced symptom was easy fatigability and weakness in the thighs and legs when walking. Loss of sustained erection was frequently an additional symptom.

INSIDIOUS THROMBOSIS OF THE AORTA

The average duration of symptoms in the ten cases was seven years, although the progression of symptoms and physical changes was not identical in each patient. The two patients with the most severe symptoms and pronounced trophic changes developed them within the shortest period of time.

DIAGNOSIS

The diagnosis may be made from the history and physical examination. The most common observation, and present in all but one instance, was the absence of peripheral pulsations, including the femoral, in the lower extremities. Of equal significance was the absence of pulsation in the abdomen below the umbilicus.

Trophic changes, such as thickening and roughening of the nails, and loss of hair were noted. Moderate pallor on elevation of the lower extremities

TABLE I

CASE	PAIN	PAIN IN HIP REGION	EASY FATIGABILITY OF LOWER EXTREMITIES	INTERMITTENT CLAUDICATION	LOSS OF SUSTAINED ERECTION	BURNING PAIN	NOCTURNAL CRAMPS	DURATION OF SYMPTOMS IN YEARS
1	+	+	⊕	+	NP	+	+	7
2	⊕	NP	+	+	NP	+	+	2
3	⊕	NP	+	+	+	NP	NP	3
4	+	⊕	+	+	+	NP	NP	6
5	+	NP	⊕	+	+	NP	NP	5
6	⊕	+	+	+	+	NP	NP	10
7	+	NP	⊕	⊕	NP	NP	NP	10
8	+	+	+	⊕	+	NP	+	10
9	+	NP	⊕	⊕	NP	NP	+	5
10	NP	NP	+	+	NP	NP	NP	12

+ = SYMPTOM PRESENT
 ⊕ = ORIGINAL SYMPTOM
 NP = SYMPTOM NOT PRESENT

TABLE II

CASE	BALLISTO- CARDIOGRAM	SKIN TEMPERATURE	OSCILLOMETRY			
			RIGHT KNEE	LEFT KNEE	RIGHT ANKLE	LEFT ANKLE
1		VERY HIGH	0.5	1.0	F	0.5
2	+	DIMINISHED	F	0	0	0
3	+	NORMAL	1.5	1.0	1.5	1.0
4	+	DIMINISHED	0	0	0	0
5	+	NORMAL	1.5	1.5	0.5	0.5
6	+	NORMAL	0.5	1.0	F	1.0
7	+	DIMINISHED	0	0		AMP
8	+	NORMAL	0.5	0	0	0
9	+	DIMINISHED	0	0	0	0
10	+	DIMINISHED	1.5	1.5	1.0	1.5

⊕ = + = CONSISTENT WITH CONDITION
 F = FLICKER OF OSCILLOMETER NEEDLE
 0 = NO PULSATION OF OSCILLOMETER NEEDLE AT ANY PRESSURE

TABLE I.—The predominant symptoms of 10 patients with thrombosis of the bifurcation of the aorta.

TABLE II.—Instrumental findings on 10 patients with thrombosis of the bifurcation of the aorta.

was another noticeable finding. Rubor and cyanosis were observed in some instances with the extremities in a dependent position. Gangrene and atrophy were usually absent, and were seen in only three of our patients. In the others, the absence of physical changes which might be expected with obliteration of such a large and important component of the circulatory bed is singularly significant. This is probably accounted for by the insidious nature of the disease and the development of abundant collateral channels.

Thrombosis of the aorta is easily differentiated from embolus to the terminal aorta. In the former, the onset is unsuspected because the symptoms are mild, while in the latter, the onset is sudden and the pain severe. In both conditions the pulsations of all vessels below the umbilicus are usually absent. Changes resulting from severe circulatory insufficiency are noted immediately in the lower extremities following embolus. Coldness to touch, hypesthesia, frequently anesthesia, and abnormal pallor become apparent immediately. In

chrombosis, these changes appear late, often years after the onset of symptoms. In both conditions, unless treatment is instituted, gangrene and ulceration are the ultimate outcome, occurring in a period of days in patients with emboli, after years in those with thrombosis.

Instrumental observations yield useful information and are included in this study to substantiate clinical evidence, but are not essential for diagnosis. Skin temperatures, oscillometry and ballistocardiograms were recorded on each patient. Ballistocardiograms of a normal person and of a patient with thrombotic obliteration of the bifurcation of the aorta are presented for com-

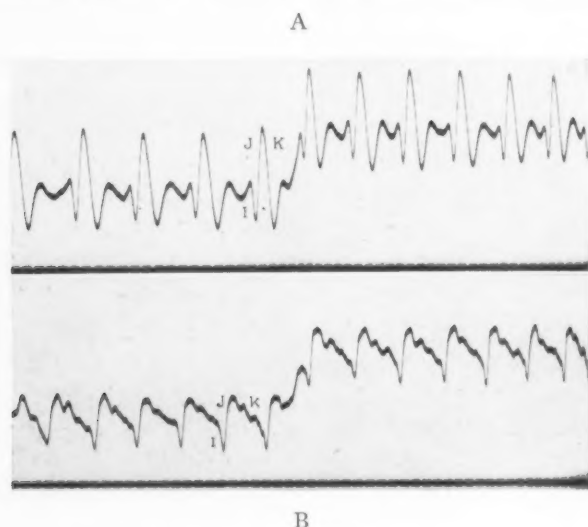


FIG. 2.—Ballistocardiogram of *A*, normal individual, and *B*, patient with thrombotic obliteration of the bifurcation of the aorta. (See footnote for explanation of wave changes.)

The Nickerson modification of the ballistocardiograph¹⁰ was used in this series. It has a low, natural undamped frequency of 1.5 cycles per second, and an incorporated critical damping mechanism. Only the deflections resulting from the initial impacts are recorded; the remainder, occurring subsequent to the ventricular systole, being "damped" out. This renders the Nickerson apparatus particularly suitable for the study of patients with thrombosis of the bifurcation of the aorta or coarctation of the aorta, since it is in these initial impacts that aberrations from the normal occur.

There are only three waves which are of significance in a ballistocardiogram of this type. The first of these (I wave) is from a footward recoil following the headward ejection of blood during ventricular systole. A greater headward deflection (J wave) then follows as the column of blood in the heart, ascending aorta, and pulmonary artery is first decelerated. A footward force, producing the K wave, follows and is due to the impact of the column of blood in the descending aorta against the peripheral resistance. It is in this latter wave that an abnormality occurs which appears to be characteristic in patients with thrombosis of the terminal aorta. In a normal individual, the slope of the curves described above approaches 90 degrees. The I wave is shallow, and the J and K waves are approximately equal in slope and magnitude. When the lumen of the terminal aorta is narrowed or obliterated, however, the column of blood in the descending aorta meets a resistance earlier and is diverted sagittally through branches and collateral channels proximal to the obstruction. The K wave therefore does not approach the baseline sharply, but tapers off irregularly, forming an angle of much less than 90 degrees with the baseline.

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parison (Fig. 2A,B. See footnote). The findings obtained on each patient by these examinations are presented in Table II.

Roentgenographic examination of the aorta in the cases so examined frequently showed extensive calcification. In two instances, an aortogram demonstrated the exact level of the site of obliteration (Figs. 3 and 4).



FIG. 3, Case 3.—Aortogram showing obliteration of the aortic lumen at the level of the second lumbar vertebra.

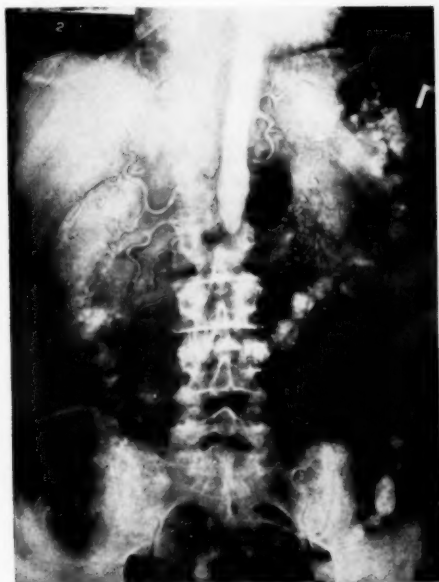


FIG. 4.—Case 10.—Aortogram (retouched) showing obliteration of the aortic lumen at the level of the first lumbar vertebra. The right renal vessels are seen, but the left renal vessels are not visualized. Collateral circulation is greatly increased.

PROGNOSIS

With any method of treatment, the prognosis is grave, due to the underlying nature of the disease. Death usually results from the complications of arteriosclerosis: coronary occlusion, uremia, or the effects of hypertension after the thrombus has extended up to and above the renal arterial orifices. It may result from gangrene and infection in the extremities. However, certain measures are frequently of value in improving the circulation and in relieving symptoms.

TREATMENT

Treatment is based on the tenets set down by Leriche. He has stated^{5, 8} that the ideal treatment would be to resect the obliterated zone and to bridge

the vascular defect by a graft. Unfortunately, the thrombosis frequently is present in the iliac arteries as well as the aorta, and surgical technics for such a procedure have not yet been perfected. The following procedures are indicated: (1) *Sympathectomy*. Bilateral lumbar sympathectomy removes vasoconstricting nerve supply to the collateral pathways below the area of sympathectomy and to the arterial trunks below the obliterated bifurcation. (2) *Resection of the bifurcation of the aorta and the thrombosed area*. This performs a two-fold purpose: it removes the thrombosis, and prevents the continuation of its formation, which otherwise would be fatal. It also removes the area of irritation which is the site for excitatory vasoconstrictor impulses which produce vasospasm in patent peripheral channels. Either or both of the above procedures are indicated in the treatment of this disease, and when both are utilized they may be performed simultaneously.

However, certain contraindications are evident for resection of the bifurcation of the aorta. Marked arteriosclerosis does not permit clamping with hemostats or obliteration with surgical sutures after division, since the vessel tears easily, and fatal hemorrhage may ensue. At operation, the extent of the thrombosis and the degree of arteriosclerosis can be determined by palpation. If the thrombosis is extensive, and approaches the renal arterial orifices, resection is contraindicated because of the technical difficulty in closing the proximal end of the aorta and at the same time maintaining function of the renal arteries. Under such circumstances, bilateral sympathectomy is indicated.

CASE REPORTS

Case 1.—W. A., a 64-year-old white male, was seen on March 17, 1948. He gave a history of 7 years duration of easy fatigability followed by pain in the hips, intermittent claudication and nocturnal cramps. This was associated with generalized arteriosclerosis and previous coronary thrombosis.

Pulsations of the abdominal aorta were absent below the umbilicus. All pulses in the lower extremities were absent. There was no atrophy of the lower extremities, and no trophic changes. There was slight pallor on elevation.

Treatment. In view of the mild symptoms and physical changes, and the hazard entailed by his cardiac disease, it was believed that surgical therapy was not indicated.

Case 2.—H. S., a 57-year-old white male, was seen on June 21, 1947, complaining of pain and burning in both lower extremities, followed by easy fatigability, severe, intermittent claudication, and nocturnal cramps, for 2 years. Four months prior to examination he developed areas of gangrene on the left foot with associated rest pain.

Pulsations of the abdominal aorta were absent below the umbilicus, and all pulses in the lower extremities were absent. There was ulceration and gangrene of the left foot, in addition to moderate bilateral atrophy, trophic changes in the skin, and rubor and cyanosis.

Treatment. The gangrene of the left foot necessitated immediate mid-thigh amputation. The stump healed poorly, necessitating re-amputation. Four months after the initial amputation, terminal aortectomy (Fig. 1) and right lumbar sympathectomy were carried out in this patient with subsequent improvement of his condition. The color of the right foot immediately improved, with increased warmth. Trophic changes in the skin regressed slightly but there was no improvement in the muscular atrophy.

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Case 3.—J. C., a 57-year-old white male, was seen on April 8, 1948. He complained of pain in both extremities, followed by easy fatigability, intermittent claudication, and loss of sustained erection, for 3 years. During the preceding two years he had developed severe, progressive, hypertensive cardiovascular disease. The patient was addicted to morphine.

Pulsations of the abdominal aorta were absent below the umbilicus, and all pulses in the lower extremities were absent. Aortography demonstrated obliteration of the aortic lumen at the level of the first lumbar vertebra (Fig. 3).

Treatment. Because of the profound hypertension, the patient's drug addiction, and because the prognosis as indicated by aortography was grave, surgical therapy was not recommended.

Case 4 and Case 5.—C. R., a 62-year-old white male, was seen on March 3, 1948. He gave a history of pain in the hips, followed by pain and easy fatigability of the lower extremities, and intermittent claudication for 6 years. The pain, initially more severe on the left, finally became more marked on the right. He had noticed mild rubor of the left foot and moderate rubor of the right foot on dependency.

Pulsations of the abdominal aorta were absent below the umbilicus, and all pulses were absent in the lower extremities. Slight trophic changes, pallor on elevation, and rubor and cyanosis on dependency of the legs were present.

O. K., a 49-year-old white male, was seen on June 19, 1947, complaining of easy fatigability of the legs, followed by burning pain and intermittent claudication, for 5 years.

Pulsations of the abdominal aorta below the umbilicus were absent, as were all of the pulses in the lower extremities. There were slight trophic changes, pallor on elevation, and rubor on dependency of the legs.

Treatment. These two patients, both physicians, were advised to submit to operation consisting of exploration of the aorta and resection of the bifurcation, if indicated, followed by bilateral sympathectomy. However, both refused operation because they felt that their symptoms were not severe enough to indicate surgical therapy.

Case 6.—P. C., a 45-year-old white male, was seen on March 8, 1948. He had had pain in the buttock and hip region followed by fatigability, intermittent claudication, and loss of sustained erection, for 10 years. Two months prior to examination he experienced an episode of syncope while serving as a blood donor. Several hours later he developed severe pain in the right foot but no discomfort in the left. The pain gradually increased in severity so as to prevent walking, and he noticed rubor on dependency of the foot.

Pulsations of the abdominal aorta below the umbilicus and all pulses in the lower extremities were absent. There were trophic changes, marked pallor on elevation, and rubor on dependency of the right foot.

Treatment. Exploration of the terminal aorta revealed it to be of the "chicken's-trachea" type, and the extension of the thrombosis, inferiorly and superiorly, with calcification, definitely contraindicated aortectomy. Therefore, bilateral lumbar sympathectomy was the only procedure carried out.

Examination one year after operation revealed that he could walk 2 to 4 blocks prior to the onset of claudication. He had been able to return to work which required him to be on his feet a great portion of the time.

Examination of the feet revealed regression of the trophic changes in the skin. No pallor was present on elevation and no rubor on dependency. The patient stated that his condition had been greatly improved by the procedure.

Case 7.—A. S., a 53-year-old white male, was seen on September 1, 1948. He had experienced claudication of both lower extremities for 10 years. His tolerance for activity had gradually diminished and one year before examination, he had sustained a burn of his left leg. The ulceration enlarged, necessitating a mid thigh amputation. The stump did not heal, and a re-amputation was performed 5 months prior to our examination. At

that time he had also developed an ulceration of the right leg, which was extremely painful and had progressively enlarged.

The amputation stump of the left leg was well healed. The right foot and toes became pale on elevation, and ruborous on dependency. An ulceration was present on the right leg. Pulsation of the abdominal aorta could be felt, but no pulsation of any vessels were palpable below the umbilicus.

Treatment. A right lumbar sympathectomy was performed. The skin surface temperatures increased, but there was very little relief of pain in the area of ulceration. The patient left the hospital before treatment was completed.

Case 8.—R. C., a 60-year-old white male, was seen on August 25, 1948. For 10 years he had suffered from cramps in the right leg on walking. One year prior to examination, his symptoms became markedly exaggerated following an illness due to food poisoning. The claudication became so severe that he was able to walk only 10 to 12 steps before developing pain on the right. He noticed back pain and loss of power of sustained erection. One month before examination he developed small, gangrenous ulcers on the third, fourth, and fifth toes of the left foot, which had failed to heal.

Numerous petechiae were present in the skin on the left foot and ankle. The foot became markedly blanched on elevation and ruborous on dependency. Similar color changes were present in the right lower extremity, but to a lesser degree. Trophic changes were present in the skin of both feet.

Treatment. A bilateral lumbar sympathectomy was performed with removal of the first, second and third lumbar ganglia. Exploration of the abdominal aorta revealed it to be thrombosed from the bifurcation of the iliacs to the level of the inferior mesenteric artery. Since calcification of the arterial wall was intense, resection of the thrombosed segment was not performed.

The ulcerations on the foot healed and the areas of gangrenous ulceration disappeared. The patient became ambulatory, and was able to return to his work, using only a cane to aid in walking. Five months after operation, he died suddenly from what was presumed to be a pulmonary embolus or coronary occlusion. No autopsy was obtained.

Case 9.—G. L., a 60-year-old white male, was seen on June 10, 1948. He gave a history of claudications in both legs for 5 years, with greatly increased difficulty during the 6 months preceding examination. Numbness, redness and increasing pain in the right foot had also been noted. There were slight trophic changes in the nails and hair of the toes. There was pallor of the right foot on elevation, and rubor on dependency. All arterial pulsations were absent in the extremities, except for a faint femoral pulse on the right.

During five months of observation he developed progressive trophic changes in the skin of his right and left feet, and an ulcer on the third right toe. On re-examination he was found to have no arterial pulsations below the umbilicus.

Treatment. A bilateral lumbar sympathectomy was performed with removal of the first, second and third lumbar ganglia. Palpation of the abdominal aorta revealed it to be thrombosed and involved in a severe atheromatous process.

Following operation, the ulceration on the tip of the third toe healed promptly, and the pre-gangrenous areas on the foot resolved. The patient was able to return to work, and has experienced greatly increased tolerance for exercise.

Case 10.—F. D., a 58-year-old white male, was seen on December 29, 1948, complaining of tiredness, weakness, claudication, and easy fatigability of his legs on activity of mild degree. Those symptoms had gradually increased in severity for 12 years.

Examination revealed no trophic changes or skeletization of the extremities. No abnormal color changes were present on elevation and dependency. No arterial pulsations could be palpated below the femoral artery, but definite femoral pulsations were present bilaterally. Pulsations of the abdominal aorta were present, but iliac pulses were not perceptible.

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An arteriogram of the aorta revealed a block below the right renal artery. There was no filling of the left renal artery, and no kidney function could be demonstrated on the left (Fig. 4).

Treatment. This patient has been advised to have a bilateral sympathectomy.

SUMMARY

The diagnostic criteria, etiology and pathology of insidious thrombosis of the aorta is presented.

The histories of ten patients are presented, and their treatment described.

A review of the literature reveals a paucity of case reports, but it is believed that this disease is more prevalent than is assumed.

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DISCUSSION.—DR. EMILE HOLMAN, San Francisco: I should like to report on four patients with obstructive calcification of the terminal aorta upon whom we have operated in the last ten years. The first one was a young woman of 45 who came to us in 1940 and who presented at operation a very thick plaque at the bifurcation without evidence of calcification, but producing complete obstruction. At the present time, she shows beginning calcification in this short segment, the only part of her body where we can demonstrate it. It is an interesting condition, probably preliminary to the

development of extensive calcification seen in three other patients. This patient had a bilateral sympathectomy and is greatly improved so far as the predominant symptoms are concerned, one of which was the constant realization that she had a very vigorously beating abdominal aorta, a phenomenon which really bothered her a great deal. Since the sympathectomy this has disappeared. Also, numbness of the extremities, extending well up to the pelvis following the slightest exertion, has disappeared.

The second patient, 56 years of age, presented herself with an indolent ulcer of the heel incident to peripheral ischemia due to calcification of the terminal aorta. This has finally healed nine months following bilateral sympathectomy.

A third patient of 65 presented the usual symptoms shown by Dr. Elkin's patients—namely, easy fatigability and calf pain on the slightest exertion. This patient also had extensive obliterative calcification of the terminal aorta and peripheral ischemia, for which a bilateral sympathectomy was done, with great improvement. Whereas before operation fatigue and pain developed after walking ten or 20 feet, she now can walk a block and more with comfort.

A fourth patient who also presented the same phenomena detailed by Dr. Elkin, was operated on by Dr. Gerbode of our clinic who also performed bilateral lumbar sympathectomy with marked improvement. It is our opinion that resection of the calcified aorta, as advocated by Leriche and his co-workers, is too hazardous for the gain obtained, and that bilateral lumbar sympathectomy will provide as much improvement as can be expected.

DR. MIMS GAGE, New Orleans, La.: I have enjoyed Dr. Elkin's paper very much and consider it most appropriate because we are seeing an increasing number of patients with Leriche's syndrome.

I recently saw a dentist less than 50 years old, who could not continue practicing because of the weakness of his legs. He had typical Leriche's syndrome—weakness of the legs, claudication in the calf muscles and increasing impotence. A bilateral sympathectomy was done. The aorta was not ligated because of the extensive arteriosclerosis.

I would like to call attention to the same type of syndrome in patients who have pronounced arteriosclerosis of the abdominal aorta with tortuosity but no thrombosis and with pulsations in the aorta, iliac and femoral arteries. The pain and discomfort in the lower extremity may be due to sympathalgia, *i.e.*, irritation of the aortic sympathetic plexus from the arteriosclerotic aortitis. It is surprising how many of these patients have systolic murmurs over the bifurcation of the aorta as well as over the external iliacs. This, of course, is due to segmental narrowing of the aorta and iliacs by arteriosclerotic plaques. Some of these patients have minor symptoms of the Leriche syndrome, whereas others have no symptoms. It will be most interesting to observe these patients over periods of time to see if the syndrome so accurately described by Dr. Elkin develops in them.

We should all be on the alert for these cases, and I would strongly advocate that we listen to the aortic and iliac arterial sounds in all patients whom we examine.

DR. NORMAN E. FREEMAN, San Francisco: We also have encountered patients with absence of pulses below the groins, and we have been able to visualize these arteries by means of retrograde arteriography, using the carotid approach. I have one slide to illustrate the fact that occasionally it is possible to have very marked obliteration and still have a small lumen.

(Slide) This patient, a man of 68, had absent pulses in both femoral areas. There was marked distortion of the aorta with almost complete occlusion. However, there is a small lumen present, and apparently the dye is able to get down through the collaterals. The middle sacral artery fills, and the left iliac artery fills fairly well from

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the right side; the other vessels are also filling. There is marked obstruction of the aorta just below the origin of the renal arteries, and yet both femorals fill through collateral vessels.

DR. FREDERICK L. REICHERT, San Francisco: This claudication business in the thigh might well be due to shutting off the lumbar segmental artery. In cutting out the coarctation of the aorta, the segmental arteries are divided. It might be well to preserve them. So in thrombosis of the aortic bifurcation segmental arteries are shut off.

I think a sympathetic innervation would be much more to the point.

QUANTITATIVE STUDIES ON THE TIME FACTOR IN ARTERIAL INJURIES*

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THE PERIOD during which an extremity, deprived of its major source of blood, remains ischemic is a factor of particular importance influencing the chance for survival upon restoration of its circulation. The disappointing results which were obtained in the treatment of arterial injuries in the leg as observed in World War II could be attributed to some extent to the considerable "time lag" or period elapsing between wounding and receiving surgical attention. Long periods of ischemia with necrosis of tissue associated with thrombosis of small arteries may produce a leg that is beyond recovery. Progress in the field of early definitive surgery was disappointing in World War II.¹⁻³ The number of immediate anastomoses of severed arteries was relatively small although an advance was made in this field as compared with the number done in World War I.⁴⁻⁶ The incidence of necessary amputation after femoral or popliteal injury treated by ligation was high.^{7, 8} In the experience of one of us, gangrene of the leg occurred after ligation of the femoral or popliteal arteries in 70 per cent of patients.⁹ It is true that not much more than ligation was possible or advisable in many instances. It must be said, however, that a vast field for improvement in the management of arterial injuries remained at the end of the war. In retrospect, several shortcomings in the overall management of vascular casualties seem to stand out after analysis of the recorded experience. In the first place it was not fully appreciated that anastomosis of the artery was essential for good results, although Blackmore strongly advocated the use of his non-suture method in battle casualties.¹⁰ A program whereby casualties with arterial wounds might be detected early and receive priority treatment was not attempted. The general lack of surgical experience with arterial anastomosis in the absence of a highly satisfactory technic applicable to all cases also contributed to the unsatisfactory end results. In a previous work we have studied several methods of arterial anastomosis in experiments in which the survival of the dog's leg depended upon one artery which had been interrupted and rejoined. The results of these experiments exonerate all types of intima-to-intima anastomosis as an important primary cause of gangrene and failure in the salvage of limbs. Our findings in these experiments performed on dogs indicated that approximately 80 per cent of legs depending on a single anastomosed artery will

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survive and be restored to nearly normal under clean wound conditions if there is no appreciable period of ischemia or "time lag."¹¹

In the present work we wish to present a study of the "time factor" in acute arterial injuries. The ideal time for restorative surgery is considered to be under six or eight hours.⁴ Not much hope has been held for the success of anastomosis procedures after this time insofar as salvaging the leg is concerned. Clinical data on the survival of human legs after various periods of acute ischemia followed by restoration of the blood supply by anastomosis is insufficient. Furthermore, the variation in the extent of the wound and the amount of functioning collateral circulation remaining in the clinical case makes an accurate evaluation of the time factor difficult as a single item. The following experiments were projected to obtain data on the survival of extremities in a series of dogs subjected to varying periods of acute ischemia under conditions which have been sufficiently standard to have significant validity.

EXPERIMENTAL METHOD

The procedure to be described was carried out on 63 dogs. Immediate mortality and death from causes not related to the leg left 57 animals for evaluation. Three separate groups of dogs were subjected to periods of acute ischemia as follows: Group I for 1 to 6 hours; Group II for 12 to 18 hours; Group III for 24 to 30 hours. A standard procedure for producing arterial injury and acute ischemia and for restoration of the circulation was used in all experiments.

The arterial injury and period of ischemia. Acute arterial injury was produced by utilizing a modification of the Halsted-Reichert leg transection replantation procedure.^{12, 13} After an especially careful skin preparation, a transection of the soft tissues of the leg was made in the mid-thigh region of anesthetized dogs. The femur, the femoral and sciatic nerves, the femoral artery and femoral vein were preserved. Anatomical replantation of the leg was then performed. At the end of this procedure the femoral artery was ligated and the vessel was effectively occluded throughout the desired period of ischemia. This preparation cuts off the main artery of supply and all collateral routes for blood via the soft tissues. Although a small amount of blood may reach the distal extremity beyond the transection by way of the medullary cavity of the femur, it is insufficient to sustain life in the leg. Previous work by Reichert¹³ and by Callow and Welch¹¹ has shown that ligation of the femoral artery in this transection replantation preparation is followed by gangrene of the leg in 100 per cent of animals. This work established the controls for the present experiments.

During the period of ischemia the wound was completely closed and the leg was encased in a plaster of Paris splint for immobilization and avoidance of contamination. During the ischemia the animals were kept at ordinary room temperature at 70 degrees to 80 degrees Fahrenheit.

The restoration of circulation. At the conclusion of the ischemic period, the ligated femoral artery was exposed under aseptic conditions. It was then

prepared for anastomosis by trimming off a cuff of adventitia. The ligated portion of the femoral artery was then excised. Thrombosis at the site of ligation was observed in less than 20 per cent of the arteries and when found was confined to the proximal segment. A good pulsating blood flow was demonstrated at the proximal end of the artery before anastomosis. The continuity of the femoral artery was restored by inserting an arterial graft between the severed ends. The suture technic was employed in all experiments. The graft was held in place by stay sutures and the anastomosis was completed by a continuous lock stitch. The technic of arterial graft was especially useful in these experiments since it permitted anastomosis with minimal tension in this situation in which a portion of the femoral artery had been excised. The use of a graft or bridging procedure is essential in the majority of clinical arterial wounds because extensive injury to the vessel involves loss of vessel substance making direct end-to-end suture difficult and hazardous. The application of arterial grafts to the problems of arterial injury was suggested to us by the recent work of Gross and his associates.¹⁴ Autografts from the opposite femoral artery were used in 16 per cent of our experiments. Fresh homografts taken from other dogs were used in 24 per cent of the anastomoses and homografts preserved for varying periods were used in 60 per cent. These preserved or "bank" homografts were stored in a fluid medium at temperatures several degrees above freezing for as long as three weeks before they were used. Anticoagulants were not administered in these experiments either during operation or in the postoperative period.

During the course of the long transection replantation procedures intravenous fluids along with transfusions of whole blood were given. An initial dose of 300,000 units of penicillin was administered prior to operation and was continued with a daily dose of 150,000 units for 7 to 14 days. At the restorative operation wounds were completely closed and no dressings were applied.

EXPERIMENTAL FINDINGS

The experiments conducted allow observations upon three aspects of the problem of arterial injury: (1) the survival of ischemic legs after restoration of circulation, (2) the effectiveness of femoral artery grafts as a method of anastomosis, and (3) the late functional results in legs salvaged after different periods of ischemia.

Influence of Periods of Ischemia on Leg Survival. Group I. The legs of 21 dogs were transected and reimplanted using the arterial graft anastomosis after a period of ischemia ranging from one to six hours. There were an approximately equal number of animals operated at the extremes of time; i.e., one and six hours. In only two animals was the leg lost, representing a 90 per cent salvage rate for this period of acute ischemia (Table I).

Group II. Of the 26 animals whose legs were transected and maintained ischemic for intervals ranging from 12 to 18 hours, 13 lost their legs. There

were approximately an equal number of animals operated at the extremes of time in this group. The rate of leg survival was, therefore, 50 per cent for the group of animals of this ischemia period.

Group III. Ten animals did not have a restoration procedure performed until after 24 hours had elapsed. Only two viable extremities were obtained, a survival rate of 20 per cent in this group. It did not seem profitable to explore the late range of this 24 to 30 hour time period in more than two of the ten animals, in view of the findings in the first eight dogs, which were done after 24 to 26 hours of ischemia. Results in these first animals demonstrated at once that the upper limit of time lag had been approached. The two legs which survived were those of dogs with ischemia for 24 and 25 hours respectively.

The legs of the dogs in all groups were pulseless and cold during the ischemic period. Skin temperatures approached that of the room in which they were exposed. The ischemic part of the leg near the transection line in the thigh was noticeably warmer than the more distal parts of the lower leg and foot since it was warmed by the adjacent vascularized tissues of the thigh.

TABLE I.—*Restoration of Circulation after Acute Ischemia*

Period of Acute Ischemia	Experiments Number	Legs Survived	
		Number	Percent
Group 1 (1 to 6 hours).....	21	19	90
Group 2 (12 to 18 hours).....	26	13	50
Group 3 (24 to 30 hours).....	10	2	20

The skin coloration varied from a marked pallor to deep cyanosis. In Groups II and III having prolonged ischemia there was a firmness and inelasticity of the muscles which was accompanied by resistance to passive motion resembling rigor mortis.

After anastomosis had been completed, the legs became warm, the color improved and other evidences of restored circulation appeared. Usually the temperature of the operated leg rose several degrees above that of the other side. The mean rise in skin temperature was 14.5 degrees Fahrenheit at the calf as determined by a surface pyrometer. The superficial veins of the leg became obviously distended. In 80 per cent of the restored legs the pulse of the anterior tibial artery was immediately palpable at the ankle. The legs of the animals in Group I were of normal size immediately following restoration while those legs in Group II and Group III presented a moderate to marked tense swelling involving the muscular tissues throughout the extremity. In the transected replanted limbs of all groups there was a progressively increasing edema. The swelling reached a maximum in the one to six hour group on about the fourth day. On about the sixth postoperative day the edema began to subside and usually it had largely disappeared by the ninth day. Reichert has shown that the disappearance of the edema accompanies the regeneration of lymphatics across the transection.¹³ In the two longer

ischemic periods there was a more rapid increase in the edema so that after 24 hours it was marked and maximal on the third day. Several days more were required for its subsidence than in the one to six hour group of animals. When wound infection was present disappearance of edema was further delayed.

Discussion of Leg Failures. The nature of the experimental procedure invited a high incidence of wound complications. The long operating time which was divided into two stages and the prolonged periods of ischemia both contributed to complications. The importance of the interval of ischemia was evident when the rate of per primum healing was examined. Sixty-two per cent of the wounds in dogs' legs subjected to only one to six hours of ischemia healed per primum while the rate in those subjected to 12 to 18 hours was 14 per cent. In those having 24 and more hours of ischemia no wound healed without complication. The extensive operative wound and the presence of ischemic tissue offered an unequaled opportunity for bacterial invasion. Positive bacterial growths were obtained from 47 per cent of the wounds that were cultured at the time of the restorative procedure in spite of all precautions used in handling these animals. None of the cultures yielded *Clostridia*

TABLE II.—*Analysis of Failures after Restorative Surgery*

Ischemic Period	Experiments	Total Failures	Graft Failures		Wound Complications (Intact Graft)
			Primary	Secondary	
1 to 6 hours. . . .	21	2	0	2	0
12 to 18 hours. . . .	26	13	1	10	2
24 to 30 hours. . . .	10	8	2	3	3
All periods.	57	23	3	15	5

or anerobic *Streptococci* and none of the legs failed because of gas gangrene. Penicillin therapy greatly reduced infection in these wounds and it is possible that without it these ischemia experiments could not have been investigated, using the present technic.

The proximate cause of leg failure in 18 out of the total 23 was some accident that befell the arterial graft used to restore the circulation. The other five failures were the direct results of wound complications at the transection site.

In Table II an analysis of the findings in legs that failed has been tabulated. The majority of the graft failures were found to be secondary to wound infection with deep abscesses and dehiscence. Thrombosis of the graft, perforation of the graft by erosion, or disruption of the anastomotic suture line were variously found. There were only three instances of primary graft failure; all of these had intraluminal thrombosis. This low incidence of primary thrombosis in the graft augurs well for their use, especially since anticoagulants were not used.

It was found that the muscle mass at the line of transection in the jeopardized portion of the extremity invariably succumbed first to the effects of

ischemia. This was due in part to the division which the transection effects of the small vessels usually supplying these muscles from above. The earlier death of these tissues, however, was not related to this factor alone, since dogs in Group I sustained the lack of this source of blood as evidenced by the rate of per primum healing and normal recovery of the legs in this group. It is probable that tissue necrosis at this level proceeds at an accelerated rate because of the higher local temperature. As the time of ischemia was extended, the degree of tissue necrosis was reflected in the greatly increased incidence of wound complications that were followed by leg failure. This finding can be explained satisfactorily only on the basis of degeneration of tissue to a point beyond which recovery was not possible after restoration of the circulation via the femoral artery.

The ischemic limbs of dogs in Groups II and III which were examined at post mortem showed grossly a softening of all the muscles, which was most evident just distal to the transection line. In those of the 24 to 30 hours group with far advanced changes there was actual liquefaction of the muscle tissues in the vicinity of the transection. In addition, liquefaction was observed to occur in the central portion of the anterior tibialis muscles. These findings are similar to the characteristic pathologic changes of early Volkmann's ischemic contracture as Griffiths has pointed out.^{15, 16} The presence of these far advanced alterations in the muscular tissue indicated that the time limits of ischemia for leg survival imposed by tissue necrosis had been approached in the time period of 24 to 30 hours during which there had been deprivation of the circulation.

It may be speculated that thrombosis in the small end arteries supplying the muscle initiated, or simultaneously accompanied, muscle tissue death and that inadequate blood reached these tissues after restoration of the femoral artery. Histological tissue studies of these animals' legs are in progress.

Arterial Graft Anastomosis. The requirement for anastomosis without tension in arterial injury in which excision or loss of some part of the vessel generally occurs is fulfilled by the arterial graft method. This technic is superior to the vein graft method in a number of respects. We believe that it is easier to perform than the non-suture vitallium tube vein graft technic of Blakemore, Lord and Stefko. The artery graft is a sturdier bridge and does not result in the narrowing of the lumen that is unavoidable when metal cuffs are employed. If autogenous grafts were an absolute requirement the disadvantage of the arterial graft technic for patients would be obvious. Suitably sized fresh autografts cannot be taken from the human subject without danger of impairing circulation to the part supplied. The development of a "bank" for arteries removed from cadavers as suggested and utilized by Gross, however, is a practical solution to this problem. The experimental conditions in the transection-replantation wound have subjected these grafts to a rigid test. In one dog in the 12 to 18 hour group which had an extensive dehiscence of over half of the tissues at the transection site which left the femoral sheath

structures suspended without support, the artery graft continued to function and to supply satisfactorily the distal leg until slow healing by granulation took place. In Fig. 1 a roentgenogram of the injected arterial tree demon-



FIG. 1.—Arteriogram in an animal sacrificed at four months showing a functioning preserved arterial homograft. Arrows indicate the site of the graft. Observe the interruption of the major collateral arterial channels produced by the previous transection procedure at the level of the graft.

strates an intact and patent graft in this same animal sacrificed when healed four months after the dehiscence. A photograph of this graft appears in Fig. 2.

There was little difference in the early and later results whether fresh autogenous, fresh homografts or preserved homografts were employed. A similar incidence of secondary graft failure occurred with all three types of grafts;

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namely, 30 per cent, 23 per cent, and 24 per cent for fresh autografts, fresh homografts and preserved homografts respectively. The three primary graft failures with thrombosis were represented by one case in each variety of graft. There was no evidence in the course of these experiments that the preserved graft is any more susceptible than the fresh graft to the stress and infection encountered with wound complications. The ready availability of the preserved grafts of several sizes from the artery bank constituted a definite convenience for this work.

Late Function. The most significant differences in late function in those dogs surviving a sufficient time for evaluation were apparent between Group I and II animals. Dogs subjected to only one to six hours of ischemia had partial use of their legs after one or two weeks and in six weeks they had all

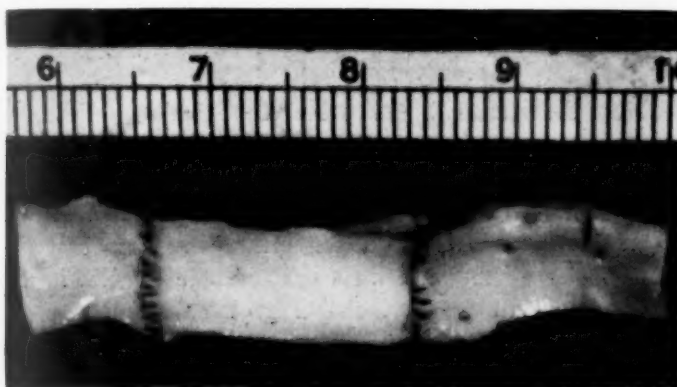


FIG. 2.—Photograph of the arterial graft shown in Fig. 1 after fixation. There is no thrombosis or erosion of the intima in this specimen.

regained nearly normal function. There was only one animal in Group I that had more than a slight weakness or slight limitation of motion, and this dog had had a postoperative abscess of the thigh which had to be drained.

When ischemia was continued for 12 or more hours, the return of function was always delayed and incomplete with limitation of motion and loss of strength as a constant finding. Response to stimulation by pin prick of the skin of the restored leg was present in these animals. The growth of hair continued in those with more prolonged ischemia at reduced rates. All had some muscular atrophy. Contractures were present in the muscles of all the late restored legs of these dogs. In a few of Groups II and III dogs, the contractures were only slight. The majority, however, had a moderate degree of contracture. In two of the animals having ischemia for 18 and 24 hours respectively, the contractures were virtually complete, producing extremities fixed in full extension. Ambulation has been good in both of these animals on a "peg leg" and the function has been surprising. The picture which these two dogs with advanced muscular contracture present is essentially similar in certain respects to that seen in the late result of Volkmann's ischemic contracture in the human subject.

DISCUSSION

The data from these experiments, projected into terms of arterial injuries in human subjects, lend support of the view that reparative surgical treatment with early anastomosis of severed major arteries of the extremity should be practiced whenever possible. The salvage of 50 per cent of limbs ischemic for 12 to 18 hours and of 20 per cent of those ischemic for more than 24 hours in the experimental animal offers decided encouragement for the recovery of human extremities with severe vascular injuries when treatment has been delayed beyond the accepted optimum time of six to eight hours. While none of the legs in the animal preparation used in these experiments escaped gangrene when the femoral artery was ligated, it has been surmised that some collateral circulation is partially intact and sufficient to prevent gangrene in approximately 30 per cent of instances when femoral or popliteal vessels have been ligated in human leg injuries in warfare. Seldom is a complete transection of the soft tissues of the leg seen in civil injuries which is a great advantage in extending the possible limits of the "time lag."

The modifying factor of the clean wound technic used throughout these experiments has, without doubt, been an advantage in favor of these animals. On the other hand, infection and dehiscence was the prime cause of leg failure after prolonged ischemia. This was a consequence in part of ischemic necrosis of the tissues but also of the experimental limitations, which, in animals, has necessitated closure of the wound with partly devitalized tissues and bacteria buried in closed spaces. In the human subject an open wound technic is possible and desirable in the contaminated wounds and much of the infection we encountered might be avoided, and secondary hemorrhage from the anastomosis in failures reduced. The experience in the last war with wound infection was surprising.

Homograft arteries have survived sufficiently long in our dogs to pass the critical period before collateral circulation becomes effective. In fact, we believe that they have a good longevity, although other investigators¹⁷ have doubted their durability. Late studies of these grafts in surviving animals are contemplated.

We believe that the arterial graft anastomosis is the best method for joining arteries of the extremities when there is loss of arterial substance, although we have no experience in human subjects. The use of banked arteries should be practical for both civilian and military hospital groups.

Survival of the leg itself with a damaged major vessel cannot be the sole desideratum; rather, the aim should be to secure a viable leg that functions as well as possible under the existing circumstances. To accomplish this it is essential that the main vascular channel be restored to function. The few long term follow-up studies of vascular casualties available indicate a sizable incidence of functional limitation in legs with femoral and popliteal injury. Even in legs with arteriovenous fistulas which are believed to have so well developed a collateral circulation that safe ligation of the femoral or popliteal vessels is

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possible without resulting gangrene, the occurrence of chronic circulatory deficiency after quadruple ligation is high.¹⁸ These legs are frequently susceptible to cold; claudication is often observed and sometimes trophic changes follow. It is, therefore, of importance to provide a permanent means of arterial restoration in the case of vascular injuries if good results are to be expected. It is difficult to compare the impaired function seen in the legs of the dogs in the present experiments with results in human subjects. As a rule the acute ischemia in the injured human leg would not be expected to reach the degree seen in these animals' legs except in the unusual transection type of wound.

Although severe muscular contractures were present in some of the legs of dogs in the longer ischemia periods, the possibility of this disability occurring in the human subject should not be a deterrent to efforts to salvage the leg. There is no method of determining slight variations in ischemia in legs with wounds of unknown extent and variable loss of collateral vessels. As long as the extremity does not show signs of gangrene or extensive tissue deterioration, attempts to restore the circulation through the damaged main vessels should be carried out. Some impairment of function can be expected in certain cases. However, such sequelae can be dealt with as they present at a later observation.

SUMMARY

In these experiments estimations have been made in animals on the probability of the survival of legs undergoing acute ischemia for time intervals of specific duration. Three time periods which extended from the onset of the ischemia to its abolition by restoring the circulation, corresponding to the clinical "time lag," were investigated. Under standard conditions of injury depriving the legs of their blood supply it was found that following restoration by arterial anastomosis the survival rate for these legs were as follows: (1) for periods of ischemia ranging from one to six hours, 90 per cent survival; (2) for periods of ischemia ranging from 12 to 18 hours, 50 per cent; and (3) for periods of 24 hours or over, 20 per cent.

Arterial grafts of three sorts were used with equal success. These were fresh autografts, fresh homografts and preserved homografts. Intravascular thrombosis in the grafts seldom occurred primarily. Failure of these grafts from thrombosis or hemorrhage was secondary to infection and wound dehiscence in all but three of 23 failures of legs to survive. The incidence of secondary failures were related to the period of ischemia. Anticoagulants were not used in these experiments.

Ischemia for a period beyond 12 hours in animals whose leg survived resulted in a variable degree of disability of the limb which was principally the consequence of contracture and atrophy.

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CLINICAL EVALUATION OF TWO TESTS FOR INCIPIENT THROMBOSIS*

PROTHROMBIN ACTIVITY AND FIBRINOGEN B OF LYONS

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THE WELL-KNOWN CLINICAL SIGNS of postoperative venous thrombosis are tenderness in the lower extremity and evidence that embolism to the lung has taken place. The latter may mean a fatal issue; the former indicates that some type of radical treatment to prevent the latter should be instituted. This treatment is, of course, anticoagulant therapy or femoral vein ligation. Neither course of action gives 100 per cent protection. Obviously what is needed is a practical test which will warn of the imminence of thrombosis or will indicate its presence in the very early stages. Some tests which have been proposed are the clotting index of Bancroft and Stanley-Brown,¹ daily determinations of the coagulation time (Bergquist²), the heparin tolerance test of de Takats and Gilbert,³ the heparin titration method of Waugh and Ruddick,⁴ decelerated coagulation time determinations (Kadish⁵), prothrombin activity of diluted plasma (Brambel and Loker,⁶ Shapiro⁷), daily prothrombin time determinations (Sandrock and Mahoney⁸) and tests for fibrinogen B of Lyons.⁹

This communication presents our experience with the last two tests. No attempt will be made to explain why the others have not been adopted in clinical practice, except to state that in addition to being apparently non-specific, most of them are time-consuming and therefore impractical to carry out as screening procedures.

Sandrock and Mahoney⁸ studied the prothrombin levels of 382 patients during the postoperative period and concluded that the findings were of value in determining which patients should receive prophylactic measures against thrombosis. Their results indicated that the stage is set for postoperative thrombosis on the second or third postoperative days, and that this tendency to thrombosis can be detected by an increased prothrombin activity of the whole plasma.

We have carried out prothrombin activity studies on 283 surgical patients. Usually, the patients were chosen for study because of the presence of factors predisposing to thrombotic complications. The composition of the group with regard to the types of operations is given in Table I. Many were in the older age group, and not a few had had a previous history of thrombo-embolism. Specific treatment, if any, was not begun until the commonly accepted clinical signs appeared. As a rule, there were nine prothrombin determinations on each patient, the day before operation, the afternoon of the operation, and daily for seven days thereafter. The one-stage prothrombin method of Quick¹⁰

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was used. A commercial brand of thromboplastin (Difco) gave a normal prothrombin time of 13 to 15 seconds. In tabulating the results, the test was considered to be positive if the prothrombin activity reached 100 per cent or above on the second or third postoperative days. The cases have been divided into two groups, namely, those with no clinical evidence of thrombosis, and

TABLE I.—Operations on the Group Studied by Prothrombin and Fibrinogen B Tests

Operation	Cases
Cholecystectomy.....	68
Hysterectomy.....	63
Gastrectomy.....	27
Colon operations.....	25
Hernia repair.....	18
Prostatectomy.....	15
Fractures.....	13
Leg amputation.....	8
Splenectomy.....	7
Nephrectomy.....	5
Miscellaneous.....	46
Total.....	295

those who were believed to have developed such a complication (Table II). In 258 patients with negative symptoms, there were 121 false positive tests. Furthermore, in more than half of the 25 cases in whom there was definite or suspicious evidence of thrombosis, there was a false negative prothrombin test.

The finding of clinical evidence of thrombosis in 25 of 283 patients (8.1 per cent) demands an explanation. It has already been mentioned that the group was weighted to some extent with regard to predisposing factors. The

TABLE II.—Correlation between Clinical Signs and Prothrombin Activity

		Cases
Signs negative—258 cases.....	{ Test negative	137
	{ Test positive	121
Signs positive—25 cases.....	{ Test negative	15
	{ Test positive	10

clinical observers were undoubtedly "thrombosis conscious" and some questionable cases may have been included. The complications were as follows: leg thrombosis, 15 cases; pulmonary infarction, with and without antecedent clinical phlebothrombosis, 13 cases; coronary thrombosis, one case. There were four autopsies in the series; three showed thrombosis which had not been suspected clinically. There was one death due to thrombo-embolism.

Case 1.—M. M., a 68-year-old woman, had a cholecystectomy for cholelithiasis. Her postoperative prothrombin activity indicated a positive test, since it was 100 per cent on the second and third postoperative days. On the 17th day, she had a pulmonary infarct. She was treated with heparin, but developed a lung abscess in the infarcted area and pyelonephritis, and expired on the 25th day from uremia. It might be argued that she

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should have received anticoagulants because of her positive test, but to be consistent we would have to have treated 121 other positive cases who never showed any clinical evidence of intravascular clotting.

The following case summary is an example of the group of cases which showed clinical thrombosis without warning from the prothrombin determinations.

Case 2.—M. H., a 62-year-old man, had a partial gastric resection on Nov. 12, 1948. The prothrombin levels on the first, second, third and fourth postoperative days were 90 per cent, 89 per cent, 80 per cent and 56 per cent respectively. On the fourth day, tenderness was noted in the left calf, and there was a positive Homans' sign. Shortly afterward he had pain in the chest. Heparin was begun, and thereafter his convalescence was uneventful.

On the basis of the experience outlined above, we concluded that in our hands the test for prothrombin activity was not specific enough to be of value in picking out patients in the prethrombotic state.

FIBRINOGEN B OF LYONS

Our interest in "fibrinogen B" was stimulated by the appearance of an article by Cummine and Lyons⁹ in *The British Journal of Surgery*. Lyons¹¹ had previously published the results of some of his blood coagulation experiments and he concluded

that the clotting of fibrinogen by thrombin occurs in at least two stages; the initial step is the liberating of blocked thiol groups in fibrinogen brought about by one component of thrombin; the second, an oxidation, probably by a naphthoquinone complex in the thrombin converting protein-SH to protein -S-S-protein (fibrin). The native fibrinogen was designated by the letter A. After it was acted upon by the component A of thrombin (not to be confused with component A of prothrombin of Quick¹²), it became fibrinogen B and was that much closer to becoming fibrin, or the true clot. Lyons' conception of the blood clotting mechanism is summarized in Fig. 1. In the first paper, Lyons used 2-methyl-1: 4-naphthoquinone to cause the fibrinogen B to gel. The test described in the second paper is as follows: A reagent is prepared by dissolving 2 Gm. of β -naphthol in 100 cc. of 50 per cent alcohol and then exposing this solution to oxygen until it turns brown. Four and one-half cc. of blood is mixed with 0.5 cc. of 1.1 per cent sodium oxalate. This is centrifuged and 1 cc. of the plasma is pipetted off into a 13 x 100 mm. tube. To this is added 5 drops of the reagent. After shaking, the mixture is allowed to stand for 10 minutes, when it is examined for clot formation. A negative and a positive test may be seen in Fig. 2.

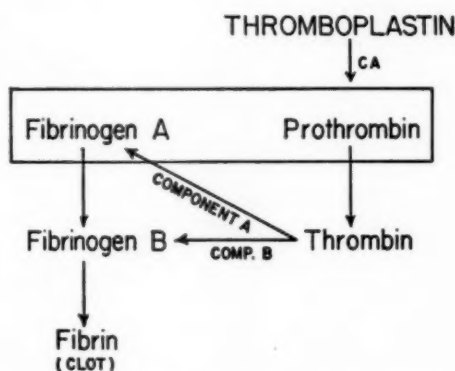


FIG. 1.—Schema of normal blood coagulation, according to Cummine and Lyons. *Brit. J. Surg.*, 35: 337, 1948.

Lyons states that both "profibrin" and fibrinogen B form a gel with the β -naphthol, but the profibrin appears only when the Fibrinogen B content is very high, and since both substances are significant clinically from the viewpoint of thrombosis, it is desirable to use the test which demonstrates both

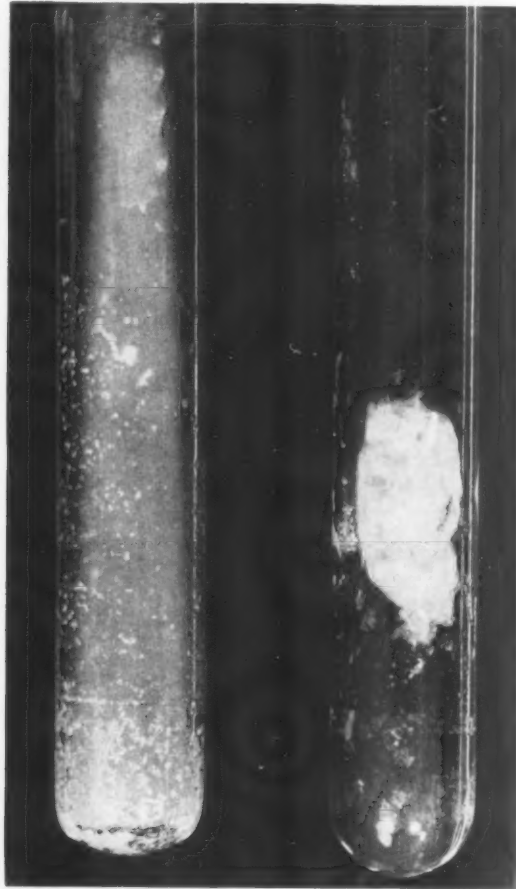


FIG. 2.—Lyons' test for fibrinogen B. An alcoholic solution of β -naphthol has been added to the plasmas of two patients. After a 10-minute interval, the tubes have been tipped to an almost horizontal position. The test on the left is negative, that on the right, positive.

substances. He states that if it is necessary to determine fibrinogen B alone, a 5 per cent aqueous solution of hydroquinone-quinhydrone should be used and the plasma examined for clot formation in 30 minutes. It should be clearly understood that we have made no attempt to investigate the validity of Lyons' test of blood coagulation or to check the chemical reactions involved.

Cummine⁹ used Lyons' test on a number of surgical patients in the Royal

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Prince Alfred Hospital in Sydney. He concluded that it is possible, by the use of the coagulation graph (Bergquist) and the fibrinogen B estimations, to subdivide patients who are to undergo surgical procedures into four groups: (1) Those patients in whom free fibrinogen B does not occur in the plasma and the coagulation graph is of normal type (*i.e.*, clotting time above three minutes by the capillary tube method). Intravascular thrombosis does not develop in these cases. (2) Fibrinogen B may be found in the plasma either persistently or intermittently, but the coagulation graph is normal. In the absence of previous thrombosis or venous stasis, thrombosis does not develop in these cases. (3) Fibrinogen B occurs in the plasma and the coagulation time remains persistently low, in the order of three to four minutes. Intravascular thrombosis appears to be inevitable. (4) No fibrinogen B appears in the plasma but the coagulation graph is low. This has been observed after an intravascular thrombosis has occurred. (Has the fibrinogen B been used up?)

TABLE III.—*Correlation between Clinical Signs and Fibrinogen B Tests*

		Cases
Signs negative—109 cases.....	{ Test negative	77
	{ Test positive	32
Signs positive—18 cases.....	{ Test negative	4
	{ Test positive	14

We carried out fibrinogen B tests on 127 postoperative patients. One hundred and sixteen of these also had the tests for prothrombin activity described earlier in the paper. It was therefore possible to observe the effectiveness of the two tests on the same patients in many instances.

The results are summarized in Table III. A little less than a third of the patients in whom no signs of thrombosis developed gave a false positive test. Eighteen patients out of 127 (14.2 per cent) were thought to have thrombosis clinically. In 14 of these, the fibrinogen B test was positive, leaving only four false negatives.

It should be pointed out again that the 18 instances of postoperative thrombosis did not develop in a general cross section of surgical patients, but in a group of thrombosis-prone patients.

Case 3.—B. F., a 35-year-old male. A spleno-renal anastomosis was carried out following splenectomy and nephrectomy for bleeding esophageal varices. The patient had further fatal hemorrhage in spite of the operation, and the autopsy showed thrombosis in the splenic vein behind the pancreas and remote from the anastomosis. The fibrinogen B test had been positive on the day of operation, and each day until the patient died. The prothrombin activity on the second day was 70 per cent.

Reference should be made to Case 2 above. The postoperative prothrombin activity was consistently below normal, but the fibrinogen B test was positive on the second, third and fourth days before clinical thrombosis was detected.

On the other hand, there were several times when the test failed to warn of impending thrombosis, as in the following example:

Case 5.—G. K. was a 44-year-old woman on whom hysterectomy was carried out. On the first postoperative day the fibrinogen B was negative. On the second day the prothrombin activity was 100 per cent (positive test). On the third day the fibrinogen B was again negative, but on this day tenderness developed in the left calf, and it was deemed urgent to begin heparin therapy.

TABLE IV.—*Results of Fibrinogen B Tests in Prothrombin-tested Patients with Clinical Signs*

	Fibrinogen B Test	Cases
Signs positive; prothrombin test negative—15 cases....	{ Negative	1
	{ Positive	7
	{ No test	7
Signs positive; prothrombin test positive—10 cases....	{ Negative	3
	{ Positive	4
	{ No test	3

It is of interest to see how often the fibrinogen B test was right when the prothrombin test was wrong, and vice versa. In Table IV, the 25 "Signs Positive" cases from the lower half of Table II have been tabulated with respect to what the fibrinogen B test showed if it was done. It is striking that of 15 cases with positive signs and negative prothrombin tests there was only one which showed a false negative fibrinogen B test.

Similarly, Table V tabulates how the prothrombin test reacted in the 18 patients with positive signs who had fibrinogen B tests. There were seven false negatives in a group of 14 cases with positive signs and positive fibrinogen B tests.

TABLE V.—*Results of Prothrombin Tests in Fibrinogen B-tested Patients with Clinical Signs*

	Prothrombin Test	Cases
Signs positive; fibrinogen B negative—4 cases.....	{ Negative	1
	{ Positive	3
Signs positive; fibrinogen B positive—14 cases.....	{ Negative	7
	{ Positive	4
	{ No test	3

As an additional study, single tests were done on 83 ambulatory individuals in the out-patient department. Only two of these showed a positive test.

CONCLUSIONS

We were unable to confirm the finding of Sandrock and Mahoney that daily determinations of the prothrombin activity of the plasma is a valuable screening test to predict thrombotic complications in postoperative patients. A somewhat more specific test is that described by Lyons which involves the

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addition of an alcoholic solution of β -naphthol to plasma. Lyons believes that the resulting gel formation is due to what he calls fibrinogen B, and that it indicates a thrombotic tendency. Further clinical and chemical investigations of this reaction are in order.

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DISCUSSION.—DR. EARLE B. MAHONEY, Rochester, N. Y.: We have been very interested in hearing of Dr. McClure's results, and are a little disappointed that he has not been able to confirm our feeling in respect to prothrombin activity.

I would like to bring you up-to-date on our experiences, as we still feel that the test has some value, in predicting postoperative thrombosis.

(Slide) This slide was presented last year. The solid line below in the graph indicates the average prothrombin activity level in patients who do not develop thrombosis. The black dots to the right of the middle line show patients who did develop thrombosis and who had an increased prothrombin activity on their third or fourth postoperative day.

(Slide) This was a summary of our cases up to the time of this meeting last year. We had investigated 309 cases at that time. Of that group there had been 4.2 per cent who had developed thrombosis. Those who had developed thrombosis had a 100 per cent increase in the activity of their prothrombin; in other words, all 4.2 per cent of these patients had increased prothrombin activity on their second, third or fourth postoperative days.

(Slide) This shows our results during the past year, in the series of patients that we have studied. We have followed 405 patients, which brings our total to the neighborhood of 800. Of these, there was no hyperprothrombinemia in 365 patients; there was an increased prothrombin activity in forty of the 405.

(Slide) Breaking down this group who had hyperprothrombinemia, there were 19 patients who did not have thrombosis. These 19 patients were primarily young individuals who were mobilized immediately after operation; also, this group comprised an interesting series of patients, those who have been operated on under tourniquets.

We have found a rather high incidence of hyperprothrombinemia in patients who have had tourniquets used during the operation, even though no thrombosis clinically develops postoperatively.

There were nine patients of the total of 40 who were given prophylactic dicumarol because of hyperprothrombinemia. Twelve patients did have hyperprothrombinemia who did not receive any dicumarol and who did develop definite venous thrombosis postoperatively.

In these 415 patients, as with the preceding 309, we have not seen a patient develop thrombosis who has not had a preceding hyperprothrombinemia.

In other words, our present evaluation of the test is that by this means we can select from all surgical patients a group who should be watched carefully and who should perhaps be given dicumarol therapy.

I would like to call attention to the fact that the determination of prothrombin activity on plasma is not specific for prothrombin, but we are merely testing the rapidity of plasma clot formation and the presence of calcium and thromboplastin. I believe last year we mentioned that because this test is positive in the whole plasma rather than in the dilute plasma, we felt we perhaps were measuring something other than prothrombin which was a precursor of this thrombosis.

We are delighted to hear of Dr. Lam's and Dr. McClure's work, because it is quite possible that this material which we are looking for may be fibrinogen B. There are many other factors which still remain to be investigated, and I am extremely interested in Dr. Lam's results.

MAJOR EDWIN J. PULASKI, San Antonio, Texas: At Brooke General Hospital my associate, Lieutenant Arthur Voorhees, and I have been studying for the past year the fibrinogen B test, and a few remarks concerning our findings at this time might be pertinent to the discussion.

First, we find that this test is considerably labile, and that there is a marked temperature effect; this means the results will be different with the plasma if the test is performed at 6° C. room temperature or 37° C. This is not stressed in the paper of Cummine and Lyons (*Brit. J. Surg.* 35:337, 1948). The highest percentage of positive tests is obtained when the experiment is carried out at 6° C.

Secondly, this test is alleged to be an indication of thrombosis which has not yet occurred but which is incipient. We find that in patients who have already developed signs of thrombosis the test may or may not be positive, but that the positive test will disappear within 24 to 36 hours after signs of thrombosis have occurred, then remain negative.

Thirdly, and perhaps most importantly, we have found that this is not a specific test for thrombosis, but it would appear to be positive, at least inconstantly so, in all cases of spreading infection. Also, this test does appear to be positive in all cases where there is considerable tissue necrosis, such as in thermal burns.

Inasmuch as it would not appear to be specific for incipient thrombosis, the fibrinogen B test of Cummine and Lyons, in our experience, does not promise to become a valuable adjunct to the clinical diagnosis of thrombosis at this stage of development of the test.

DR. CONRAD R. LAM, Detroit: I have very little to add. I appreciate Dr. Mahoney's remarks, and I think our two series could come a little closer together if we were better agreed on what constitutes hyperprothrombinemia.

INCIPIENT THROMBOSIS

If you will remember his first slide, there were a number of black dots indicating hyperprothrombinemia just above the 100 per cent line, and they were put up there because the person holding the stop watch clicked it just about a tenth of a second sooner. Our technicians do not claim to have that good a reaction time, and the surgical residents who try to perform this test usually record the prothrombin time in terms of half a second rather than trying to get any closer. Our laboratory reports nothing higher than 100 per cent, although they have obliged us by reporting the time in seconds also.

I am glad to hear that someone else is trying to see if there is anything to the fibrinogen B test, and Major Pulaski's observations are very interesting. Dr. Lyons, in his article, stresses that the test is positive in cases of infection, and a number of other conditions. Dr. Margulis, who did most of these tests, reported to me that the very vigorous centrifuging of blood to get the plasma, instead of letting the cells settle out, tends to produce a false positive test.

PHYSIOLOGIC STUDIES IN CASES OF STRICTURE OF THE COMMON BILE DUCT*

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MY INTEREST in the treatment of strictures of the common and hepatic bile ducts dates back to 1924. From that time until January 1, 1949, I have operated on 186 patients for stricture of the extrahepatic ducts. I have divided these cases into two groups: (1) a series of 98 cases in which operations were performed from 1924 through 1939 (Table I), and (2) a series of 88 cases in which 113 operations were done from 1940 through 1948 (Table II). Lewis, Friedell and I reported on the first group in three papers in 1940 and 1942.^{1, 2} In the study of this second group I have had the help of my first assistants, Drs. Spencer Phillips³ and John Cameron, and Dr. Joseph Berkson of the Section on Biometry and Medical Statistics of the Mayo Clinic.

In the first series, the hospital mortality rate was 10.2 per cent and in the second series it was 3.4 per cent (or 2.6 per cent on the basis of 113 procedures). This reduction in mortality rate, I think, can be directly attributed to a better understanding of the pathologic physiology of the liver in cases of biliary obstruction and the institution of adequate methods of treatment before, during and subsequent to operation in order to compensate for the disturbances, rather than to any particular improvement in the technic of the surgical procedure. There are, perhaps, a few exceptions to this statement; the first is that I have been able to find remnants of extrahepatic ducts above the stricture more frequently in the second series of cases than in the first, because I have searched more diligently for them; even incising the parenchyma of the liver. The same is true of the identification of the lower end of the common duct. For this reason the proportion of duct-to-duct anastomoses to those of a duct to the duodenum has increased. In 11 of the 27 cases of stricture in which I performed operations in 1948, choledochcholedocostomy was performed, in 13 hepaticoduodenostomy, in 1 choledochoduodenostomy and in 2 hepaticostomy. The incidence of duct-to-duct anastomosis in 1948 was 40 per cent in contrast to 11.2 per cent in the cases from 1924 through 1939 and 18.6 per cent in the cases from 1940 through 1947. Assuming that an anastomosis of the end of the duct to the intestine is possible, the problem that will concern the surgeon is whether to anastomose the stump of the duct to an opening made in the duodenum or to one of the loops of the jejunum. With the latter procedure the duct is anastomosed to the jejunum either with an enteroanastomosis or with a Roux-Y type of anastomosis, as recommended by Allen⁴ and Cole.⁵

Before considering this question, let me return briefly to a discussion of the pathologicophysiological changes associated with biliary obstruction and the

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preoperative and postoperative methods directed to their treatment. Although I would like to discuss tests of liver function, time does not permit more than saying that studies of the response of the prothrombin time of the blood to vitamin K, the amount of serum globulin and its relation to the serum albumin have proved in our experience, the most practical indicators of the degree of

TABLE I.—*Results According to Operation: Stricture of Common and Hepatic Ducts; 1924 Through 1939*

Operation	Cases	Well When Last Heard From		Recurrence of Biliary Obstruction		Hospital Deaths		Subsequent Deaths	
		No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent
Common duct to duodenum	34	28	82.4	2	5.9	1	2.9	3	8.8
Hepatic duct to duodenum	31	13	41.9	8	25.8	2	6.5	8	25.8
Duct to duct	11	6	54.5	2	18.2	1	9.1	2	18.2
Hepaticostomy	9	2	22.2	2	22.2	3	33.4	2	22.2
Transplantation of external biliary fistula	9	2	22.2	4	44.5	1	11.1	2	22.2
Other	4	1	25	2	50.0	1	25
Total	98	52	53.0	18	18.4	10	10.2	18	18.4

liver damage associated with a stricture. If the blood contains globulin in excess, and an elevated prothrombin time does not promptly return to normal after the administration of vitamin K, more than the average amount of injury to the liver parenchyma is likely to have occurred. The frequency with which intrahepatic biliary block may simulate extrahepatic block must be remembered in all cases in which jaundice occurs; and this is especially important when

TABLE II.—*Types of Operation for Stricture of Biliary Ducts: 1924 Through 1948*

Type of Operation	1924-1939		1940-1947		1948	
	No.*	Per Cent	No.†	Per Cent	No.†	Per Cent
Duct to duct	11	11.2	16	18.6	11	40.7
Hepatic duct to duodenum	31	31.6	39	45.4	13	48.2
Common duct to duodenum	34	34.7	10	11.6	1	3.7
Hepaticostomy	9	9.2	11	12.8	2	7.4
Other	13	13.3	10	11.6
Total	98	100	86	100	27	100

* Number of patients.

† Number of operations.

jaundiced patients have had previous operations on the biliary tract. The concentration of blood lipids are increased in the presence of obstructive jaundice and decreased in the presence of severe hepatic injury. When hepatic damage has occurred, the concentration of gamma globulin in the serum is increased and that of serum albumin is decreased. These findings are extremely reliable and the tests are not difficult to perform.

At the Mayo Clinic all patients who have jaundice are hospitalized for at

least three days prior to surgical intervention. In this period, study of hepatic function is made and the patient is prepared for operation by administration of vitamin K or some other similarly acting substance and a forced increase in the intake of carbohydrate and protein. In addition, parenteral injections that are necessary are given. If the prothrombin time is elevated and is not reduced after administration of vitamin K, blood transfusions are employed before operation. I cannot remember a single case of stricture of the bile ducts in which I have refused to operate when recurrence of the stricture has taken place, regardless of how deeply jaundiced the patient was or how many previous operations had been performed for correction of the biliary stricture. I mention this not to emphasize particularly the success that may be obtained by a properly performed procedure, even after as many as three to five previous unsuccessful attempts at repair, but to illustrate that reduction of the hospital mortality rate in my two series of cases can be attributed mainly to recent preoperative and postoperative study of the patient and his liver, institution of treatment indicated by this study both before and after operation, and the performance of a proper surgical procedure which completely relieves the biliary obstruction.

In recent years the question of effect of regurgitation of food and of gastric, duodenal and pancreatic secretions into the biliary ducts has been a matter of considerable speculation and some study. I have followed carefully all of the patients on whom I have operated since January, 1924, that is, for 25 years. In my experience now with approximately 118 cases in which the common or hepatic duct has been anastomosed to the duodenum (in 65 for more than ten years), I have been unable to prove that any reflux from the duodenum was productive of either asymptomatic or symptomatic infection of the liver. A similar observation was made on animals by Soupoult in France.⁶ Moreover, in my patients, when fever or jaundice with and without pain has led to speculation on this possibility, reoperation has always shown recurrence of the obstruction, usually of a considerable degree, at the site of the previously performed hepaticoduodenostomy, choledochoduodenostomy or choledochocolicostomy.

Of the 98 patients operated on from 1924 through 1939, 34 had sufficient duct above the stricture to anastomose it accurately to the duodenum. When these cases were studied by Lewis, Friedell and me in 1940, 82.4 per cent of these 34 patients were living and well. This group of cases, as well as the entire series, is under intensive investigation to determine the percentage in which obstruction has been cured for ten years or more.

Roentgenographic studies of the duodenum and anastomosed duct after the oral ingestion of barium have shown both air and barium in the ducts, to a greater or less degree in the cases in which the anastomosis was not obstructed. On the other hand I have found recurring obstruction, when, because of pain or fever with or without jaundice, I have reoperated on patients who have had a previous operation or operations for stricture and who have not had this reflux of barium or air from the duodenum into the common

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or hepatic ducts. In a few cases even though air and a small amount of barium were noted in the ducts, attacks of pain with or without fever, and mild transient jaundice, have occurred. At operation, contraction of the duct, sometimes to a few millimeters in diameter at the site of the anastomosis, has been found in these cases.

I presented two examples of this before the members of the Chicago Surgical Society at their meeting in Rochester, Minnesota, on January 19, 1949. I shall only mention one of these cases here, however. In this case I performed hepaticoduodenostomy 11 years ago at which time only a fringe of hepatic duct was found to anastomose to the duodenum. The patient was well for ten years and then had attacks of biliary colic with questionable slight jaundice of skin and sclera. At operation, contraction of the duct at the site

TABLE III.—Results According to Operation for Stricture of Common and Hepatic Ducts: 1940 Through 1947

Operation	Total Cases	Hospital Deaths		Cases Traced*	Well When Last Heard From		Recurrence of Biliary Obstruction		Died Elsewhere	
		No.	Per Cent		No.	Per Cent†	No.	Per Cent†	No.	Per Cent†
Common duct to duodenum	9	0	0	7	5	71.4	1	14.3	1	14.3
Hepatic duct to duodenum	32	1	3.1	25	16	64.0	3	12.0	6	24.0
Duct to duct.....	12	0	8	4	50.0	4	50.0	0
Hepaticostomy.....	8	1	12.5	6	0	5	83.3	1	16.7
Others.....	4	0	4	4	100.0	0	0
Total.....	65	2	3.0	50	29	58.0	13	26.0	8	16.0

* Patients operated on too recently for judgment of results and cases in which follow-up information was not available at this date are omitted.

† Per cent of cases traced.

of the anastomosis had reduced the lumen to a few millimeters in diameter. Plastic enlargement of the stoma was carried out and the patient has been well since.

The operation, anastomosis of the end of the biliary duct to the duodenum, when the lower segment of the duct cannot be found, is a relatively simple operation compared to that required to anastomose the duct to the jejunum. The simplicity of choledochoduodenostomy or hepaticoduodenostomy makes these procedures my operations of choice since many of the patients on whom I operate have had at least one unsuccessful attempt at repair (Table III). In point of fact, of the 27 patients I operated on during 1948, one had five previous procedures on the biliary tract, four had four, six had three, nine had two, and seven had one operation (Tables IV and V).

I have seen identical symptoms, that is pain, chills, fever or jaundice alone or in various combinations, not only in cases of contracture at the site of the biliary-duodenal anastomosis but also in cases of contracture of anastomosis between the reconstructed ends of the common duct. This brings up the question as to whether, in order to preserve the mechanism of the sphincter of Oddi at the lower end of the common duct and to prevent reflux of duodenal con-

tents into the biliary tree, it is worth while to subject the patient to diligent search for the end of the common duct below the stricture. It is debatable whether stricture does not recur more frequently when the continuity of the duct itself is re-established than when the proximal end of the duct is anastomosed to the duodenum. This problem is being investigated at present. Of

TABLE IV.—*Analysis of Procedures (Operations): Author's Series, 1948*

Operation	Cases	Prosthesis Used		
		T Tube	Polythene Tube	Catheter
Duct to duct.....	11	7	..	4 (McArthur)
Hepatic duct to duodenum.....	13	7	6	..
Common duct to duodenum.....	1	..	1	..
External hepaticostomy.....	2	2
Total.....	27	14	7	6

course the type of end-to-end anastomosis employed will make a difference in the number of recurrences when ductal continuity has been re-established. In all circular anastomoses, concentric contraction tends to occur whereas after an angulated anastomosis, that is, in one in which triangular shaped ends are sutured, concentric contraction does not occur. Unfortunately, as a rule, insufficient duct ends are present to perform an angulated anastomosis. Therefore, the problem usually is to determine what type of indwelling casting or

TABLE V.—*Relation of Number of Previous Operations to Procedure: Author's Series, 1948*

Procedure	Cases	Previous Operations				
		1	2	3	4	5
Duct to duct.....	11	6	3	1	1	..
Hepatic duct to duodenum.....	13	1	3	5	3	1
Common duct to duodenum.....	1	..	1
External hepaticostomy.....	2	..	2
Total.....	27*	7	9	6	4	1

* 6 previous operations by author.

tubing will prevent contracture of the circular type of anastomosis and how long it should remain in place to accomplish this purpose. McIndoe⁷ has stated that a period of three months is necessary to prevent contracture of tubular grafts of skin. In my opinion three months is the minimal period that splinting tubes should be kept within the common duct and from six to twelve months is probably better. Any tube used to splint the ductal anastomosis will sooner or later have its lumen occluded by bile pigment and salts and will obstruct the duct unless removed. I have removed Vitallium and rubber tubes from the common duct which were filled and encrusted with bile pigment or salts and which could not pass the sphincter of Oddi. A rubber catheter, most of which extends beyond the sphincter of Oddi into the duodenum, has seemed the best type of splint to me. It can be held in place for as long as desired by a silk thread passed through it and attached to the surface of the skin as

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recommended by McArthur. When the silk suture is removed, intestinal peristalsis will pull the catheter into the duodenum and it will pass through the intestinal tract without stopping or obstructing. Tubes of rubber, Vitallium, or polythene can be used in a choledochoduodenostomy or hepaticoduodenostomy. Bile, however, accumulates in the lumina and about the exterior of rubber and Vitallium tubes. This happens less frequently when polythene tubes are used. These tubes will pass spontaneously into the duodenum in a few weeks unless fixed in position with the long silk suture used to fix a catheter.

In the surgical procedure, I employ an upper right rectus incision. I have been able to see no clinical indications that a general anesthetic or combined nitrous oxide, ethylene, oxygen and ether is disturbing to liver function and have preferred this type of anesthesia. I keep the dissection close to the under surface of the liver; I extend it as far laterally as possible and expose Morrison's pouch. From this starting point the dissection is carried mesially until the structures of the hepaticoduodenal ligament are reached. It is then carried from the mesial part of the right lobe of the liver at a deep level to the hepaticoduodenal ligament in order to expose the hepatic artery. After exposure of the hepatic artery in the hepaticoduodenal ligament, it is nearly always possible, by upward traction on the under surface of the liver and by dissecting along the hepaticoduodenal ligament into the hilus of the liver, to find the proximal stump of the common or hepatic duct of sufficient length to use in an anastomosis either to the lower part of the duct or to the duodenum. This I was able to do in 25 of the 27 cases in which operations for stricture of the biliary ducts were performed in 1948.

SUMMARY

A study of the 186 cases of stricture of the common and hepatic bile ducts in which operations were performed, has given evidence of the beneficial effects of studies of liver function and preoperative and postoperative treatment directed toward compensating for the disturbances resulting from the biliary obstruction. Prevention of bleeding has been accomplished by the administration of vitamin K and blood. As a result, the syndrome of hepatorenal insufficiency does not occur. More diligent search for both ends of the duct beyond the stricture has been productive of a greater percentage of cases in which anastomosis of the duct to the duct or the duct to the duodenum could be accomplished. As an indication of the benefits of this routine the mortality rate of 10 per cent in the 98 cases in which operation was performed from 1924 to 1939 inclusive has been reduced to 3.4 per cent in the 88 cases in which operation was performed from 1940 to 1948 inclusive. If the mortality rate in the last group is figured on the basis of operative procedures, since reoperations were performed for recurrence of the stricture in some cases, it is only 2.6 per cent.

During these years evidence accumulated indicates that after a biliary-duodenal anastomosis, reflux of food (barium or air) into the common and

hepatic ducts is not responsible for pain, fever or jaundice but that these symptoms are the result of recurring obstruction of varying degree at the site of the previously made anastomosis. This is important because of the simplicity and ease of these operations in comparison to the operation needed to anastomose the duct to the jejunum, especially if the Roux-Y principle of jejunal anastomosis is used.

Studies are under way to determine whether results of anastomosing the ends of the duct are as good, better or worse than those of anastomosing the proximal end of the duct to the duodenum. Involved in this problem is the fact that concentric contraction occurs at the site of most circular or tubular ductal anastomoses to a greater or less degree unless prevented by a tubular prosthesis until the usual period of such contracture has passed. Whether this applies to a greater degree in anastomosis of duct to intestine remains to be determined. Hence the question arises whether in order to preserve the function of the sphincter of Oddi an operation should be performed which may be followed by a higher incidence of recurring obstruction at the anastomosis than follows choledochoduodenostomy.

To prevent contracture of a circular biliary ductal anastomosis, a rubber catheter extending from the hepatic duct into the duodenum may be used as a splint. The catheter which will be pulled into the duodenum by peristalsis can be maintained in position by a silk suture passing through it and brought out to the skin where it is anchored to a button as advised by McArthur. Other short tubes, even of Vitallium, placed within the duct will have their lumina plugged and obstructed by bile and bile will accumulate about them. This foreign body will obstruct the common duct unless removed, for they will not pass through the sphincter of Oddi. Hence they should not be used. Prostheses of any type used to prevent contracture in anastomosis of duct to intestine will likewise become obstructive agents if they remain in place too long. Fortunately this practically never occurs because they will pass into the intestine within a few weeks unless prevented from doing so by fixation with a silk suture brought to the exterior.

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INTRAHEPATIC CHOLANGIOJEJUNOSTOMY FOR BILIARY OBSTRUCTION — FURTHER STUDIES*

REPORT OF FOUR CASES

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ANASTOMOSIS OF one of the intrahepatic biliary ducts to the jejunum following a partial resection of the left lobe of the liver for certain extensive benign strictures of the extrahepatic biliary system was described in a previously published article.¹ The procedure was suggested for those cases in which the usual methods of biliary reconstruction had proved inadequate. Experimental studies and a report of a case in which this method was used successfully were presented.

Three additional patients have since been treated by this procedure and it is the purpose of this paper to review our experience with the operation.

TECHNIC

A V-shaped bilateral subcostal incision extending farther to the left than to the right, used in all cases, gave satisfactory exposure. Extension of the incision to the right of the mid-line permitted mobilization of the entire left lobe of the liver. Although all patients had been subjected to at least three previous right upper abdominal operative procedures, adhesions in the left upper part of the abdomen were not numerous and mobilization of the left lobe of the liver from the diaphragm and the surrounding structures was readily accomplished. The diameter of the intrahepatic duct isolated for the anastomosis was indicated by the size of the catheter which could be passed into the duct: Case 1, No. 14 French catheter; Case 2, No. 14 French catheter; Case 3, No. 20 French catheter; Case 4, No. 18 French catheter. Smaller ducts, of course, were present, but if the incision was carried deep enough into the liver to expose a major branch of the intrahepatic biliary system, a duct of the desired caliber was found to be available in these adult patients with chronic biliary obstruction (Figs. 1 and 2).

The major intrahepatic ducts lie in the inferior or caudal half of the substance of the left hepatic lobe, at times quite near the inferior surface. As the hepatic incision was carried into the middle third of the substance of the left

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lobe, a dense fibrous cord which contains a major branch of the intrahepatic biliary system was encountered. This fibrous cord was located without undue difficulty as it is much firmer than the surrounding hepatic tissue. Before dividing this structure, additional length of the duct for anastomosis was obtained if the cord was freed distally by curetting away the surrounding hepatic tissue. Since the fibrous cord, however, contains a branch of the hepatic artery and a branch of the portal vein, it was incised with caution. Bleeding from the artery and the vein must be controlled without encroaching on the

FIG. 1



FIG. 2

FIG. 1.—Cut surface of left lobe of liver with catheter in intrahepatic duct. Roux type jejunal segment mobilized for anastomosis. Note position of duct opening immediately beneath the level of the anterior abdominal wall.

FIG. 2.—Anastomosis completed. Antimesenteric border of jejunum being sutured to superior surface of liver. End of catheter, which passes through the anastomosis, can be seen protruding into wall of jejunum.

lumen of the duct. For positive identification, a catheter was passed proximally into the duct and bile was aspirated before the anastomosis was begun.

A careful mucosa-to-mucosa anastomosis of the duct to the jejunum was greatly facilitated by the excellent exposure and accessibility of the end of

the duct provided by the technic. Instead of attempting to suture structures located deep in the hilar region of the liver, anastomosis of the duct in this procedure was performed just beneath the level of the anterior abdominal wall. As many as 14 interrupted 00000 silk sutures were placed about the circumference of the anastomosis for accurate approximation of the mucosal layers.

The length of one side of the wedge-shaped segment was determined by the depth of the selected duct from the anterior edge of the liver. The incision was continued in such a manner as to remove a segment of hepatic tissue so that the anastomosis might be readily performed and so that the intestine would not be acutely angulated when it was placed over the cut hepatic surface.

A rubber catheter passing from the duct into the intestine was, in the past, sutured into the anastomosis with catgut. It has been felt, however, that this is unnecessary, and that the catheter might become a source of difficulty at a subsequent time should it not be passed.

A Roux segment of defunctionalized jejunum was used in the later cases rather than the jejunal loop described in the original operation. This single limb facilitated the operative procedure and probably provided a more completely defunctionalized intestinal segment than did the jejunal loop with a proximal enteroenterostomy.

POSTOPERATIVE COURSE

A satisfactory explanation is not available for the marked rise in the serum bilirubin which occurred during the first postoperative week in three of these cases. The serum bilirubin returned to an approximately normal level within four weeks after operation in two cases but did not return to the normal range for two months in the other two cases. There was a moderate drainage of bile-colored fluid from the incision during the first few days after operation in all the cases, but such discharge stopped promptly after removal of the intraperitoneal drains. Daily elevations of temperature occurred in all the cases for at least two and a half weeks after operation.

Postoperative complications developed in two patients. A large intraperitoneal abscess, presumably resulting from a previous exploration, was inadvertently opened during the operation in Case 3. Subsequent drainage of five large intraperitoneal abscesses was required. In addition, a high intestinal fistula, which developed through a former operative scar, was treated by constant suction and it closed spontaneously. Severe, unexplained bleeding into the gastrointestinal tract, with repeated passage of tarry stools during the second and third weeks after operation, occurred in Case 4. Erosion of the jejunal mucosa by the catheter in the biliary-jejunal anastomosis was suggested as the cause of this hemorrhage. Repeated transfusions were given and the bleeding stopped spontaneously. Three months after operation this patient was readmitted to the hospital deeply jaundiced and died within a few hours. At postmortem examination, the cholangiojejunal anastomosis was widely patent and was well healed. There was free communication of the right and the

TABLE I

Case No.	Date Operation	Postoperative Complications	Survival	Remarks
1	4/2/1947	None	2 years	Well 22 months. Recent upper abdominal abscess and external biliary fistula which healed spontaneously. Severe cerebral arteriosclerosis. Biliary drainage adequate at present.
2	3/20/1948	Multiple intra-abdominal abscesses. High intestinal fistula.	13 months	Prolonged, difficult postoperative course. Occasional attacks of cholangitis. Now well. Has bile in stools. Serum bilirubin slightly elevated.
3		None	11½ months	Well since operation.
4	9/14/1948	Unexplained hemorrhage into gastrointestinal tract.	3 months	Slow recovery but jaundice cleared completely. Patient well until onset of fatal attack homologous serum jaundice.

left main intrahepatic ducts at the hilus of the liver. The extensive destruction of the hepatic cells seen in the microscopic sections of the liver was compatible with a diagnosis of homologous serum hepatitis, and this was considered to be the cause of death (Fig. 3). Evidence of a spreading cholangitis was not discovered. A brief summary of the four cases is given in Table I.

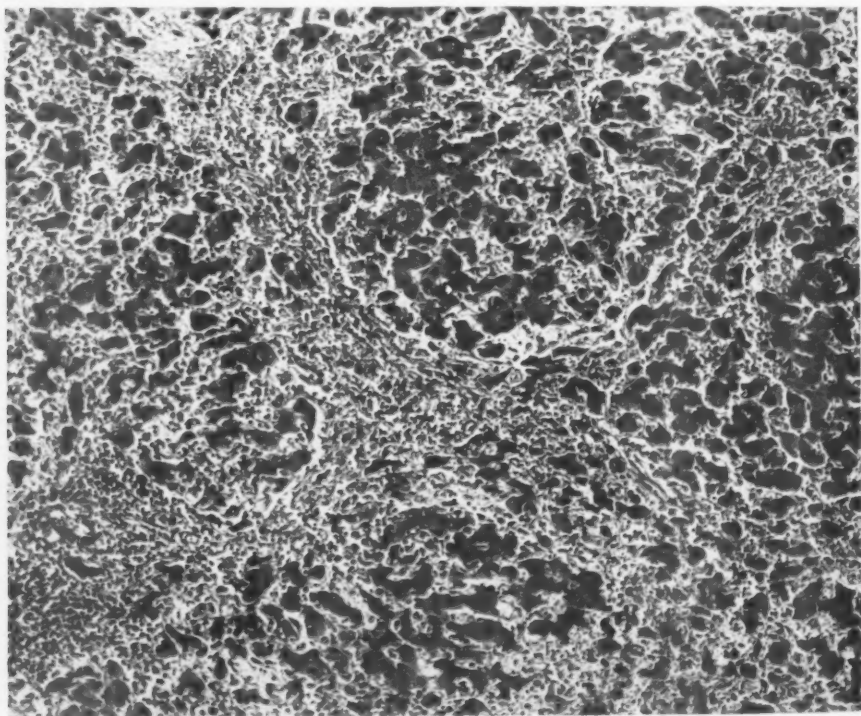


FIG. 3.—Photomicrograph of liver in Case 4 at the time of death, three months after operation, showing acute hepatic necrosis compatible with homologous serum jaundice.

DISCUSSION

Walters and Phillips² state that 20 per cent of patients operated on for repair of stricture of the bile duct will require another operation because of the recurrence of biliary obstruction. Lahey,^{3, 4} Cattell,⁵ and others have emphasized the difficulties encountered in secondary biliary repairs, such as extensive scarring in the region of the hepatoduodenal ligament, the obliteration of landmarks, and the destruction of the proximal end of the common bile duct or of the common hepatic duct.

Numerous methods have been devised for the treatment of these difficult recurrent cases of biliary stricture; all, however, have involved reexploration of this densely scarred and distorted hepatoduodenal region in which there is the ever present danger of serious injury to the portal vein or the hepatic artery. When the upper end of the common hepatic duct is extremely short or nonexistent it is difficult to perform an accurate mucosa-to-mucosa anastomosis in this area, regardless of the method used.

Our experience with cholangiojejunostomy was encouraging in all four of the cases in which the procedure was attempted. Mobilization of the left lobe of the liver was accomplished without undue difficulty. Bleeding from the cut surface of the liver was satisfactorily controlled by the mattress sutures described in the original technic.¹ The size of the intrahepatic ducts, the thickness of their walls, and the accessibility of the ends of the ducts made it possible to perform accurate mucosa-to-mucosa anastomosis with the jejunal segment in all cases. Other surgeons^{2, 3} have successfully utilized the procedure in instances of extensive extrahepatic biliary obstruction.

It is not known what result may be expected to follow this operation if the obstruction in the biliary system extends high enough to block the communication of the left and the right main intrahepatic ducts.

However, Lahey⁴ reported successful anastomosis by Doctor Cattell of the left hepatic duct when it was impossible to find the right because of the depth of the scarred duct within the liver. Atrophy of the right lobe and enlargement of the left occurred with adequate maintenance of hepatic function. If only a portion of the intrahepatic biliary system is to be drained, our experience would suggest that partial hepatectomy and cholangiojejunostomy be considered.

Since our unsuccessful experience with this procedure in infants with congenital biliary strictures,¹ the method has not been further pursued in such cases.

SUMMARY

Intrahepatic cholangiojejunostomy with partial hepatectomy was used in four adult patients in whom extensive benign biliary obstruction recurred as a result of failure of the usual methods of biliary reconstruction.

In all cases it was technically possible to perform a satisfactory cholangiojejunal anastomosis. In the selected cases in which the procedure was indi-

cated it had three advantages over the usual methods of repair: (1) Less scarring and fewer adhesions were encountered in the left upper part of the abdomen than in the right. (2) After exposure of the intrahepatic duct its superficial position in relation to the anterior abdominal wall facilitated the performance of an accurate anastomosis with the jejunum. (3) There were not any vital structures to be avoided in the immediate operative area, such as the portal vein and the hepatic artery.

One patient has been entirely well for 11½ months following operation. Two patients have been greatly improved (one for two years, the other for 13 months) but have had intermittent difficulties related to the abnormality of the biliary tract. One patient died three months after operation as a result of homologous serum hepatitis. He had made a complete recovery from the operation and was well at the time of onset of the fatal illness.

The procedure should be considered in certain cases of extensive destruction of the extrahepatic biliary system if previous reconstructive procedures have failed.

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DISCUSSION.—DR. RICHARD B. CATTELL, Boston: Mr. President and Members of the Association: Dr. Walters has had a large experience in the repair of traumatic strictures of the bile ducts and as a result his report today is of particular interest to all surgeons interested in this problem. The most impressive thing has been the improvement of results in his last series of cases and particularly during the past year, for which he is to be congratulated.

There are two general operative methods that can be utilized to repair common duct strictures. The first is the anastomosis of the proximal biliary duct or ducts to some portion of the gastrointestinal tract. Dr. Walters has employed this in approximately 80 per cent of his cases and prefers an anastomosis to the duodenum. The second method of repair is the anastomosis of the proximal duct or ducts to the distal duct, thus restoring the continuity of the biliary tract with preservation of the sphincter of Oddi.

It seems to us after the experience that Dr. Lahey and I have reported on several occasions with the treatment of over 250 of these strictures that it is possible in most instances, irrespective of the amount of damage or amount of duct removed, to accomplish a duct to duct anastomosis. As a result of this the number of cases in recent years in which we have accomplished repair by anastomosis to the gastrointestinal tract has markedly decreased. As Dr. Lahey reported before this Association last year, there is enough of the duct within the pancreas that can be dissected up and utilized to bridge a wide defect.

Comparing our experience with that of Dr. Walters, we find that our repairs are about the reverse of his in that we do duct-to-duct anastomosis in about 80 per cent.

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In the smaller number of cases in which the duct is anastomosed to the gastrointestinal tract, we prefer to utilize an antecolic loop of jejunum with diversion of the tract by proximal entero-enterostomy.

We are at present completing a follow-up study of our cases and find 80 per cent satisfactory results in the duct-to-duct anastomoses, whereas there has been over a 30 per cent recurrence of symptoms in patients who have had the duct anastomosed to the jejunum.

It is surprising that it has taken us all so many years to appreciate the fact that reflux of contents from the gastrointestinal tract into the common duct is not responsible for recurrence of symptoms in these cases except rarely. In this, we concur with Dr. Walters. If recurrent symptoms occur after an initial period of freedom of symptoms, one can be assured that there has been a recurrence of duct obstruction.

In light of our experience, we would urge that a better search be made for the lower end of the common duct in the pancreas, and in spite of the fact that occasionally, even after finding such a duct, it will be impossible to utilize it, for the most part, duct-to-duct suture by this method is a feasible method of repair of these strictures.

Dr. Longmire's beautiful presentation of his ingenious operation of intrahepatic anastomosis of the left hepatic duct to the jejunum is of considerable interest. In view of the massive adhesions he found in the right upper quadrant in his cases, he chose this method rather than to attempt to find duct remnants. It seems to me that there are two possibilities of relief of symptoms in his cases. The first implies that there is a stump of common hepatic duct left which permits the right hepatic duct to drain through the short segment of common hepatic duct and drain back through the left duct which has been anastomosed. If this is true, there is probably enough common hepatic duct to accomplish some anastomosis directly. The second possibility is that only the left lobe of the liver is being drained. I should like to call attention to an experience we have had in six patients in whom only one hepatic duct was anastomosed when the other duct could not be found within the hilum of the liver.

Surprisingly enough, with one lobe of the liver drained, two of these patients have had good results, but this has been followed by extensive atrophy and shrinkage of the opposite lobe, as we have determined on re-exploration. Based on this experience with six cases of anastomosis of one hepatic duct, I think we will need to reserve judgment on this type of operation until we have autopsy findings on these cases to show that we are actually draining both ducts by the operation which Dr. Longmire proposes.

Dr. THOMAS H. LANMAN, Boston: We at the Children's Hospital agree with Dr. Walters' theory about retrograde cholangitis. In our cases of congenital anomalies of the bile ducts in which we have been able to anastomose either the hepatic or the common duct to the duodenum, we do not find that retrograde cholangitis is a problem.

In our series, some cases of which have been followed for 18 to 20 years, if there is an adequate stoma, these patients do not exhibit evidence of a retrograde infection. In doing an anastomosis in these small patients it is likely that the stoma is relatively much larger than in an older patient and, of course, there is no sphincter of Oddi. We, therefore, feel that an obstructive element is the cause of retrograde cholangitis, and not a large stoma.

Dr. WARREN COLE, Chicago: It is rather apparent from the discussion of these two papers that we must be familiar with several different types of operations when we deal with a stricture of the common duct.

I think Dr. Longmire's procedure is one which will definitely be of value in many cases. I have used it, but only in one patient in whom I could not find a duct at the hilum except at a distance of almost two inches within the liver. We cut across the left lobe

of the liver and encountered a fairly large duct which was anastomosed to a loop of jejunum.

I agree with Dr. Walters that cholangitis is in general an expression of obstruction. However, we have had two patients in whom we think we have proved that reflux did cause the cholangitis. Early in our work we anastomosed a loop of jejunum to the hilar duct in five patients, four of whom had poor results with persistence of chills and fever. I reoperated two of them within a few weeks but found the stoma between the duct and jejunum entirely patent. Since x-ray examination with barium revealed regurgitation, I decided to interrupt the ascending loop going to the hilus of the liver. The chills and fever stopped and both patients promptly got well. They had immediate relief from their chills and fever, merely by prevention of the regurgitation. We are definitely of the opinion that reflux was the cause of the cholangitis particularly since we did nothing to the stoma.

I want to call attention to a remark Dr. Cattell just made on the ability to find perhaps only one duct at the hilus. We have had an experience like that in one patient; unfortunately, we found only the left hepatic duct. After looking futilely for the right duct, I anastomosed the jejunum to the left hepatic duct. Strange to say, this patient made a very satisfactory recovery and has had no symptoms whatsoever, except that she has retained a mild jaundice but with no chills and fever. I don't know what is going to happen, but she has progressed satisfactorily for two years. Dr. Cattell remarked about atrophy of the other lobe of the liver, when its duct remains completely obstructed for a prolonged time. I don't know when this would take place, but already in our patient the left lobe has enlarged and the right has receded in size.

DR. FRANK H. LAHEY, Boston: Dr. Cattell has said practically everything we would like to say regarding our experiences with bile duct strictures, but I would like to add one or two things from the relatively large experience we have had with this very difficult problem that may be helpful to anyone who has to operate upon patients with such strictures.

I think none of us is going to fail some time or other to have to deal with these problems, and anything that anyone can add that will be helpful, just as Dr. Longmire has helped in the development of his ingenious procedure, is going to be worth while.

These bile duct strictures are difficult problems. The search for the injured ducts in the scar tissue of many of these patients who have been operated upon so many times is, to say the least, a trying and a very serious problem. I would like to add just a few things out of these experiences which may be helpful to anyone operating upon patients with such strictures or duct defects.

I do not know of anything more worrisome in these cases than to open the portal vein, but having done it at least six times, I would like to give anyone comfort by saying that the pressure in the portal vein is low, and that with good exposure the portal vein can be controlled by quite rough suture. I do not think that it is something which you would want to practice every time you repair a bile duct stricture, but it is comforting, particularly at the height of the difficulty, to know that largely it is controllable.

Another thing that has arisen in my experience and in Dr. Cattell's and Dr. Marshall's is that we have hesitated to reoperate immediately upon these patients when they have been sent to us within a short time after the injury has taken place because of the fear of soiling and because of the bleeding and the oozing, but that is in some cases a more desirable time to operate on them than later. If you operate upon these patients soon after they have had their ducts injured, you will often have the best chance of finding cut ducts easily. The reason is that there is not then the firm scar and fixation which will be found later; the ducts are still flexible, and while the oozing and soiling make the operation anything but beautiful, they are not harmful and apparently do not interfere with the end result.

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I must also reiterate that we have had to learn the very hard way to find these cut ducts in very dense scar tissue and adhesions, and I am delighted that Dr. Walters has said that he is now able to find them. It means you must turn the duodenum over. You must go through all the troublesome oozing that comes from the little vessels along the edge of the mobilized duodenum. You must split the head of the pancreas. This cut pancreas bleeds distressingly, and you think it will never stop, but it always does with pressure and ligature, and with patience you can find the lower end of the duct and can, in most cases, so mobilize it that the severed ends can be approximated.

One other thing I would like to bring to your attention is the fact that in almost all cases you can fulgurate out the common hepatic or right and left hepatic ducts from within the surface of the liver. Dr. Cattell has just successfully anastomosed the cut ducts in one of these patients who had had eight previous operations. I have just sent one patient home with a successful anastomosis who had seven previous attempts at repair. With patience and exposure, you can find most of these ducts and anastomose the ends.

We believe these anastomoses, particularly of the hepatic and common ducts, should be supported by a dowel in the form of a T tube for at least a year or 14 months. It is very undesirable to put the T tube through the line of anastomosis, but if you can put it below or above and have a limb of the tube go through the anastomosed area, which can and sometimes does stricture, you then keep this area open for at least a year, and I think you then have a much better chance of permanent patency of the anastomosis.

DR. WALTMAN WALTERS, Rochester, Minn.: I want to congratulate Dr. Longmire on his excellent contribution to the surgery of stricture of the extrahepatic bile ducts.

I thought you might be interested in a cholangiogram (Fig. 1) which confirms what Dr. Longmire said regarding the communication between the right and left intrahepatic biliary tree. The patient whose cholangiogram is shown in Fig. 1 was a woman on whom I operated twice for stricture of the common duct and was unable to find any extrahepatic duct. I inserted a rubber catheter of small size through the parenchyma on the superior surface of the left lobe of the liver into a dilated hepatic duct. The intrahepatic communication of the biliary ducts is evident in the cholangiogram and it is evident that if the left hepatic duct were anastomosed to the jejunum as Dr. Longmire has shown, drainage of bile from both lobes could be obtained.

I am of the opinion that permanent results of duct-to-duct anastomosis are not going to be as good as those following anastomosis of the duct to intestine because of the danger of contracture on anastomosis of the ends of the ducts. Results were excellent in 82 per cent of my first series of cases in which the duct was anastomosed to the duodenum, in contrast to 55 per cent in which the ends of the duct were joined. (Slide)

In the second series results were practically identical; they were excellent in 50 per cent of the cases in which duct-to-duct anastomosis was employed and in the other 50 per cent of these cases symptoms recurred. The percentage of excellent results was as high in cases in which choledochoduodenostomy was employed in my second series as in the first series. The similarity of these percentages in both series is significant, I believe.

Physiologically it would seem better to anastomose the duct to the duct in order to preserve the mechanism of action of the sphincter of Oddi than to anastomose the duct to the duodenum. I believe, however, that contracture is going to follow this circular type of anastomosis in more cases than we would suspect. A nonabsorbable foreign-body splint cannot be used within the common bile duct without its having to be removed later. Bile will accumulate in the interior and around any splint in the duct, whether it is a vitallium tube, a polythene tube or a rubber tube. Furthermore it will

not pass through the sphincter of Oddi unless sufficient length of tube extends beyond the sphincter so that it will be pulled out by peristalsis.

In 1923 Dr. McArthur of Chicago suggested the use of a rubber ureteral catheter to serve as a temporary splint for the common duct. It extends through the sphincter of Oddi, but is maintained in position with a silk suture passed through it and brought to the exterior of the body where it is anchored to a button. I have used this method in innumerable cases in which I have employed duct-to-duct anastomoses. I have kept the catheter in for as long as a year, and I think it is preferable to the T tube because



FIG. 1.—Complete stricture of the extrahepatic bile ducts. Cholangiogram was taken after a catheter had been introduced through the periphery and superior surface of left lobe of liver into a dilated hepatic duct. Cholangiogram shows communication between left and right intrahepatic ducts.

when the T tube is pulled out, the opening left in the duct closes by contractive fibrosis with scarring of the duct.

I think we must concentrate now on determining whether or not duct-to-duct anastomosis, and all it entails, gives superior results, which have not been apparent in my groups of cases, to the anastomosis of the duct to the intestine, and whether the anastomosis of jejunum to the stump of the common duct either with jejunojejunostomy

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or a Roux-Y jejunostomy gives results superior to the more easily performed biliary duodenal anastomosis. It has been my pleasure to present the results of such operations in my cases.

DR. W. P. LONGMIRE, JR., Baltimore: Mr. Chairman, I wish to thank the discussants and to say that we have been greatly influenced in the development of this procedure by the ideas that Dr. Walters has expressed for a number of years, namely, the importance of performing a careful mucosa-to-mucosa anastomosis, and the importance of such a careful anastomosis in preventing subsequent cholangitis.

We do feel that in the left hepatectomy procedure it is possible to obtain a better exposure of the end of the duct and to perform a more accurate anastomosis than would be possible when working deep in the hilus of the liver.

We have been influenced also by the statements of Dr. Cole, Dr. Allen and others, in regard to anastomosing the duct to a defunctionalized portion of the intestinal tract, and that accounts for the use of the Roux jejunal segment in this procedure.

We are very heartened to hear of Dr. Cattell's experience with anastomosis of the left hepatic duct at the hilus of the liver. We have previously carried out some investigations to determine the portion of the liver which is drained by both the right and the left ducts, and feel that even if the obstruction were high enough to block the communication of the two ducts, a condition which we think occurs very infrequently, there is still enough liver tissue drained by the left duct that an anastomosis of this duct with the jejunum would provide adequate biliary drainage. Such seems to have been the experience in Dr. Cattell's cases. Thank you very much.

DEPERITONEALIZATION: CLINICAL AND EXPERIMENTAL OBSERVATIONS*

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ONE OF THE generally accepted principles of abdominal surgery is that areas denuded of peritoneum should be reperitonealized prior to closure of the abdominal cavity after celiotomy. The reason for this is the belief that such denuded areas are very likely to become the points of adhesions for loops of bowel which shortly thereafter are more firmly attached because of fibrous tissue organization of the exudate that develops between the serosa covered bowel and parietal or other area devoid of peritoneum. Such attachments are believed to favor angulations and torsions which in turn might cause intestinal obstructions.

In radical excisions of various types of large intra-abdominal neoplasms it became necessary in many instances to remove large areas of both anterior and posterior parietal peritoneum and the conditions were such that reperitonealization of the denuded areas was not possible, so that they were left bare.^{1, 2} No instances of postoperative intestinal obstruction have so far been encountered due to adhesions alone after several months to years following these operations. When obstructions have been observed, as indeed they have, months to two or more years after operation, the cause has been invariably recurrence of neoplasm in the mesentery of the bowels or between intestinal loops. Not only have anterior and posterior parietal areas been left denuded, but in over 45 instances of complete excision of pelvic viscera the entire true pelvis was stripped of its peritoneal covering, the small bowels permitted to descend into the pelvis and come into contact with the musculo-fascial and osseous surfaces of the pelvic parietes, and there have been no instances of postoperative obstruction due to adhesions.

Furthermore in over 20 additional instances where the bladder and internal female genitalia were removed with conservation of the rectal colon, but no reperitonealization carried out, there have been no intestinal obstructions. In over a hundred radical panhysterectomies with pelvic lymph node dissections and no reperitonealization of the lateral pelvic areas and areas previously occupied by the uterus and broad ligaments, there have been no instances of postoperative intestinal obstructions due to adhesions.

Failure of reperitonealization was at first not intentional, but resulted from the fact that there was not sufficient peritoneum remaining because of the wide

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resection necessary to excise the several types of neoplasm. It must be admitted that some misgivings prevailed at first concerning subsequent complications due to adhesions that were expected to occur. These complications did not materialize.

A series of experiments were carried out in dogs to observe what might develop in the peritoneal cavity after large areas were stripped of peritoneum or where the abdominal wound was closed without approximation of peritoneum.

EXPERIMENTAL

Dogs of both sexes and of varied breeds were employed. Operations were carried out under the usual aseptic precautions with nembutal anesthesia.

Dog 16:

May 24, 1948. Segments of peritoneum on anterior abdominal wall were resected (also omentectomy and splenectomy), 14 by 4½ cm., on each side of mid-line. Fig. 1A.

July 7, 1948. Celiotomy; no adhesions; denuded areas were smooth and glistening. Another area of anterior parietal peritoneum, 4 by 3 cm., was resected.

July 13, 1948. Exploratory celiotomy; no adhesions.

Sept. 24, 1948. The dog was killed. There were no adhesions to the denuded areas; the latter appeared smooth and glistening as if reperitonealized. Fig. 1B.

Dog 17:

May 28, 1948. A segment of the anterior parietal peritoneum was removed, 14 by 12 cm.

July 9, 1948. Celiotomy. There were a moderate number of fibrous adhesions between bowel and denuded area. There was lysis of adhesions.

Aug. 18, 1948. Celiotomy. A segment of anterior parietal peritoneum about one silk suture was removed. Several loops of small bowel were attached to the upper third of the denuded area; the remaining portion of the latter was smooth and glistening.

Sept. 17, 1948. The animal was killed. The area site of resected stitch: smooth and glistening. There were many adhesions between the loops of small bowel and anterior abdominal wall.

Dog 18:

May 28, 1948. A segment of peritoneum 15 by 14 cm. was excised from anterior abdominal wall. The animal was killed 41 days later. There were no adhesions. The denuded surface was again smooth and glistening, and had the gross appearance of being covered with peritoneum.

Dog 20:

June 15, 1948. A segment of peritoneum 14 by 14 cm. was excised from the anterior abdominal wall.

July 23, 1948. Celiotomy was again performed. One loop of bowel 2 by 4 cm. was fixed to the anterior abdominal wall. The remaining portion of denuded area was smooth and glistening. Adhesion was broken.

Aug. 20, 1948. Celiotomy. The denuded area was now smooth and glistening.

Aug. 28, 1948. Died (eventration). The denuded area was smooth and glistening.

Dog 22:

June 23, 1948. A segment of anterior parietal peritoneum 14 by 14 cm. was excised.

Aug. 23, 1948. Celiotomy. Adhesions between bowels and denuded area were present, but most of the latter seemed to have become reperitonealized.

Dog 021:

Nov. 23, 1948. A segment of peritoneum 12 by 15 cm. was excised from the right anterior parietal region.

Jan. 1, 1949. Celiotomy. No adhesions; denuded area was smooth and glistening; appeared to have become reperitonealized.

A



B

FIG. 1.—*Dog 16.* (A) Photograph of two large segments of anterior parietal peritoneum each 14 by 4 to 5 cm. stripped from either side of midline celiotomy wound. (B) Photograph of excised segment of anterior abdominal wall taken at necropsy 4 months after initial deperitonealization and two and one-half months after second stripping of reformed peritoneum. Note smooth glistening surfaces to which there were no bowel adhesions. A new layer of peritoneum had reformed in this area.

Dog 02B3:

Nov. 26, 1948. A segment of peritoneum 7 by 10 cm. was excised from the left anterior parietal region.

Jan. 12, 1949. Celiotomy. An area 2 by 1 cm. of inferior pole of spleen was adherent to the denuded area; the remainder of the denuded area was smooth and glistening. The

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area was denuded November 26, 1948, and was again denuded of smooth glistening "peritoneum."

Feb. 25, 1949. Celiotomy. A small area of omentum (1 by 1 cm.) was slightly adherent to the previously denuded area. Bowels were not adherent. The denuded areas were smooth and glistening.

Dog 02B2:

Nov. 26, 1948. A segment of peritoneum 7 by 12 cm. was excised from the mid-anterior abdominal wall.

Jan. 1, 1949. Celiotomy. Seropurulent fluid was found in the abdomen. Three loops of small bowel were lightly adherent to the denuded area and were readily freed. Areas of bowel adhesions measured approximately 4 by 2, 1 by 1½, and 2 by 1 cm.

March 4, 1949. Celiotomy. No adhesions were noted. The denuded areas were smooth and glistening.

Dog 02B4:

Nov. 26, 1948. A segment of peritoneum 12 by 10 cm. was excised from the left anterior abdominal wall.

Jan. 19, 1949: Celiotomy, no adhesions. The denuded area was smooth and glistening. It had the appearance of being covered with peritoneum.

Dog 02B13:

Jan. 19, 1949. A segment of peritoneum 8 by 7 cm. was excised from the mid-portion of abdominal wall.

Feb. 2, 1949. The dog was killed by another dog. There were no adhesions of bowel to the denuded area; there was one thin adhesion of omentum to the denuded area. Fig. 2.

Dog 02D7:

Dec. 3, 1948. The omentum, spleen and tail of the pancreas were resected. The wound closed without approximation of the peritoneum.

Jan. 26, 1949. Celiotomy, no adhesions were present to the under surface of laparotomy wound.

Dog 02D10:

Dec. 13, 1948. Spleen, omentum, right kidney and adrenal were resected. The wound closed without approximation of peritoneum.

Feb. 2, 1949. Celiotomy, no adhesions were found beneath the previous wound.

Dog 02D13:

Jan. 28, 1949. Cholecystectomy. The wound closed without approximation of peritoneum.

Feb. 11, 1949. Celiotomy. There were no adhesions to the previous wound; the underlying loops of bowel were free.

DISCUSSION OF EXPERIMENTAL RESULTS

The least radical disruptions of the peritoneal surfaces are represented by Dogs 02D7, 02D10, and 02D13, in which the celiotomy wounds were closed without closure of the peritoneum at all, as a separate layer. While the series is small, re-examination revealed, 54 days, 51 days and 14 days after the initial operation, no evidence of fibrous or fibrinous adhesions of bowels to the region of the operative wound, where peritoneum had not been approximated.

In ten instances large segments of peritoneum were excised and subsequent reoperation in several weeks revealed no adhesions between bowels and denuded areas in six of the animals. In four instances there were adhesions.

In Dog 17, there were moderate fibrous adhesions between bowels and deperitonealized area 42 days after the denudation. These were severed, and at a third celiotomy, 40 days after the second, the adhesions had not recurred except for one at the site of a silk suture in the abdominal wall. At necropsy, 30 days after the third operation, many fibrous adhesions had again formed between bowels and anterior abdominal wall. In Dog 20 a large area (14 by 14 cm.) had been deperitonealized, and 38 days later only one loop of bowel over an area 4 by 2 cm. was adherent to the denuded area. Twenty-eight days after

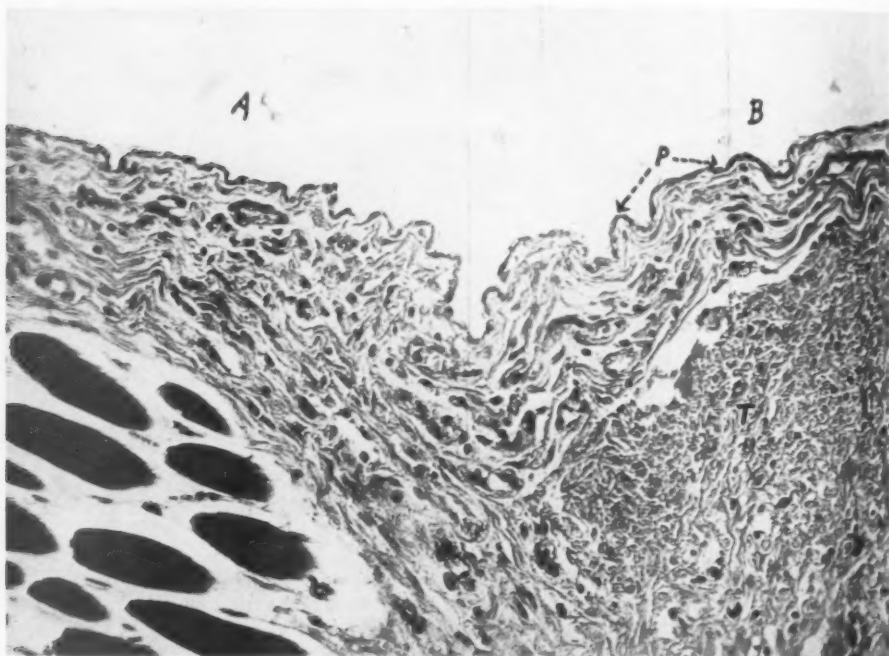


FIG. 2.—Dog 02B13. Photomicrograph of junctional zone between A, undisturbed peritoneum and, B, area (8 x 7 cm.) deperitonealized two weeks previously. The dog had been killed accidentally by another animal and the deperitonealized area was smooth, glistening and presented no adhesions. Note P, distinct layer of peritoneum in previously deperitonealized area. T, newly found fibrous tissue in area previously stripped of peritoneum.

this had been liberated no adhesions were found, and the whole of the originally denuded area had become smooth and glistening. In Dog 22, there were fibrous adhesions between bowel and denuded area 61 days after the deperitonealization. The adhesions found in Dog 02B2 probably were stimulated, in part at least, by the chronic peritonitis present. The marked healing tendency of the peritoneum is well illustrated by Dog 02B3, where one denuded area 10 by 7 cm. was created and found smooth and glistening 47 days later, at which time the same area was again denuded of reformed peritoneum and, at the third operation 44 days later, the area again found to be smooth and glistening without adhesions to underlying loops of bowel.

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Microscopic examinations were made of sections taken through the areas denuded of peritoneum and which, weeks later, exhibited smooth glistening surfaces with what seemed to be reformation of a new peritoneum (Fig. 2). There was loose vascularized connective tissue in these areas over which a membrane had reformed, one cell in thickness. The latter cells were flattened and appeared identical with the peritoneum in the intact adjacent areas where denudation had not been carried out. The mode of formation of the new peritoneum was not investigated in detail, and undoubtedly was derived from one of two sources or from both, viz., (1) proliferation of peritoneal cells from adjacent undeperitonealized areas to cover the defects, and (2) condensation of fibroblasts from the subperitoneal tissue to form new peritoneal cells in response to a functional demand.

One feature would appear to be of special interest, and that is the situation in human patients where all of the musculo-fascial components of the abdominal wall are excised, leaving skin and subcutaneous fat only to constitute the abdominal wall. During the months following such procedures the abdominal wall appears to have become thickened, denser and less elastic, indicating that the fibrous tissue elements of the abdominal wall in these areas have proliferated to add strength to the abdominal wall. No hernial sacs develop, due undoubtedly to the lack of a narrow defect in an otherwise more rigid wall, the latter conditions obtaining when there is a limited separation of the deeper layers in an abdominal wound that was closed in the conventional manner, as occurs in the usual development of a postoperative incisional hernia.

Two specific examples may be cited:

Case 1.—M. D., age 53 years, admitted to Memorial Hospital in January, 1948, complaining of pain in the right abdomen, where there was also a palpable mass, obviously recurrent neoplasm invading the right abdominal wall. He had previously received an excision of the cecum for carcinoma with ileo-transverse colostomy, in another institution.

On March 16, 1948, celiotomy was performed and the recurrent carcinoma excised, together with the musculo-fascial and peritoneal components of the right lower portion of the abdominal wall, 70 cm. of ileum that was adherent about the recurrence, the lower third of the right lobe of the liver, the upper ascending and right third of the transverse colon, and an elliptical portion of the wall of the second (descending) portion of the duodenum together with the mesenteries corresponding to the excised portions of bowel and the right kidney and ureter and retroperitoneal tissues. An ileo-transverse colostomy was done. The abdominal wound was closed and over most of the right abdomen the parietes consisted of only skin and subcutaneous fat.

Convalescence was complicated by (a) infection of the upper portion of the wound (but no dehiscence), (b) thrombophlebitis right calf and small pulmonary infarct. He was discharged on the 42nd day. In a few weeks he returned to work and subsequently gained 35 pounds in weight.

He was readmitted July 21, 1948, for drainage of an abscess in the right abdominal wall.

By the end of a year the abdominal wall in the region where it was constituted by only skin and subcutaneous fat was, of course, more flaccid than the opposite side and yet served very well as a parietes. Except for some bulging there was no frank herniation, Fig. 3.

On March 3, 1949, he was readmitted with clinical signs and symptoms of small bowel obstruction. Celiotomy was again performed through a right paramedian incision, and this incision was almost entirely in the area in which the abdominal wall was constituted by skin and subcutaneous fat. When the peritoneal cavity was entered there were no adhesions between the anterior parietes and the underlying loops of small bowel. The area on the right side from which all peritoneum had been stripped a little over a year previously was now observed to be covered by a smooth glistening surface which appeared

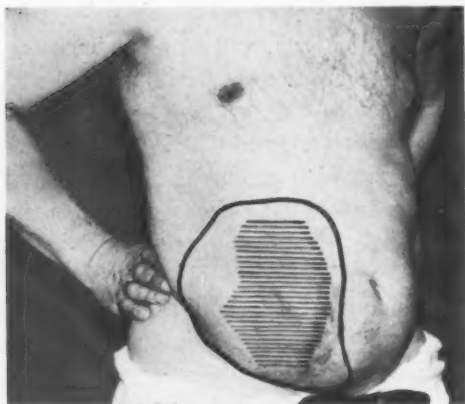


FIG. 3

FIG. 3.—Case 1: M. D. Photograph of anterior abdominal wall approximately one year after excision of recurrent carcinoma of ascending colon that had invaded the anterior abdominal wall. Large circular marking on skin indicates the approximate extent of resection of the musculo-fascial components of the abdominal wall, and in this area the parietes were composed of skin and subcutaneous fat only. There was moderate bulging but this in no way interfered with patient's general condition, and he returned to work full time and gained 35 pounds in weight. Shaded area indicates approximate region denuded of peritoneum. A year later the patient was again operated upon for intestinal obstruction, which was found to be due to small recurrence constricting loop of ileum. No adhesions were observed between bowels and previously deperitonealized area (See Figs. 4 & 5).

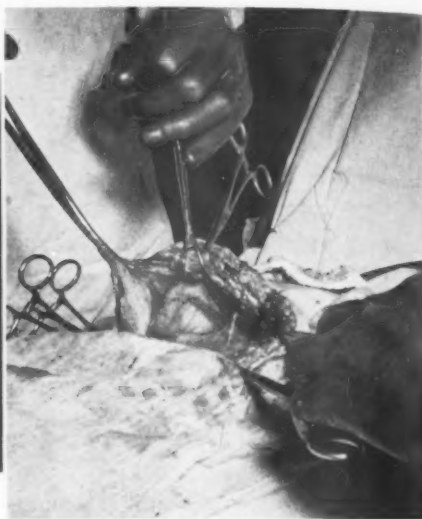


FIG. 4

FIG. 4.—Case 1: M. D. Photograph was taken at celiotomy performed one year after previous excision of recurrent carcinoma of ascending colon invading right abdominal wall. At the previous operation musculature, fascia, and anterior parietal peritoneum over a large area of the abdominal wall had been excised, and the abdominal parietes in the region consisted only of skin and subcutaneous fatty tissue. (See Fig. 3). The above photograph was taken after a right paramedian incision. The lateral edge of the wound is readily elevated, revealing no adhesions to underlying bowel, and there has been a reformation of smooth glistening transparent surfaces identical in appearance to peritoneum.

to resemble peritoneum and, to all intents and purposes, appeared to be a new peritoneal layer that had become reconstituted in situ or by growth from adjacent peritoneal zones (Fig. 4). Strips of this reperi-tonealized tissue were excised for fixation in formalin, and sections cut for study. Fig. 5, a photograph of one of the sections, shows the presence of a veritable peritoneum.

The obstruction was found in the small bowel near the ileo-colostomy, and was due not to adhesions but to a disc-shaped mass of recurrent neoplasm that had "glued" two loops of the small bowel together with marked constriction of the lumen of one of the

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loops. Resection of the involved loops, together with more mesentery and the right half of the remaining transverse colon with the old ileo-colostomy, was carried out, and a new anastomosis between lower jejunum (or upper ileum) and transverse colon just proximal to the splenic flexure was performed.

Convalescence was satisfactory except for a limited wound infection.

The situation in the patient described above is quite comparable to the experiments carried out in dogs, where peritoneum was excised over large areas and where, at subsequent celiotomy, no adhesions were found between underlying loops of small bowel and the denuded parietes, and where reformation of a peritoneum-like membrane occurred over the denuded area.

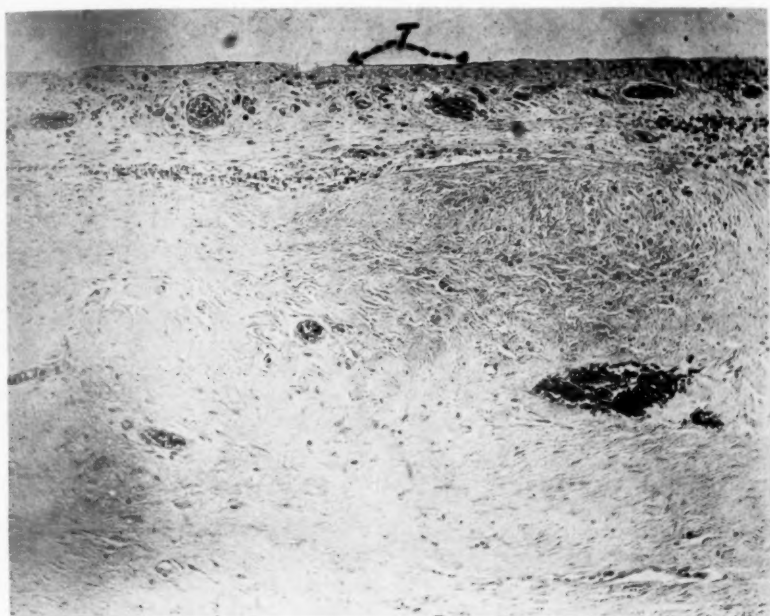


FIG. 5.—Case 1. Photomicrograph of peritoneal aspect abdominal wall which one year previously had been excised en masse with recurrent carcinoma of ascending colon. The abdominal wall after this operation consisted of skin and subcutaneous fat only. Note T, distinct layer of peritoneum that has appeared over deep surface of subcutaneous fat that was exposed to the peritoneal cavity.

Another instance of good functional abdominal parietes following extensive resection of musculo-fascial and peritoneal components is afforded by the following patient.

Case 2.—M. Y., female, age 23 years. She previously had several successive resections of a neoplasm in the right lower quadrant of the abdominal wall that recurred repeatedly. Histologic diagnosis: Sarcoma, pleomorphic. Roentgenray therapy had also been given.

On June 27, 1947, a wide resection of the musculature and fascia of the right lower abdominal wall was carried out, the incisions encompassing widely the gross limits of the tumor. When the peritoneal cavity was entered it was observed that the cecum and ascending colon were adherent to the deeper surfaces of the tumor. Accordingly a right hemi-colectomy was performed en masse with the segment of right abdominal wall. Closure of the wound was carried out in such a manner that only skin and subcutaneous fat formed the abdominal wall over a large area of the right lower parietes. The general

condition was very satisfactory after operation, and during the ensuing months the portion of abdominal wall mentioned above became somewhat rigid and did not bulge unduly when the patient coughed. She was seen again a year and a half after the initial operation; she was six months pregnant and roentgenograms of the chest revealed diffuse metastases in both lungs. General deterioration had not yet begun to manifest itself. The right lower portion of the abdomen continued to appear firm and there was no excess bulging (Fig. 6).

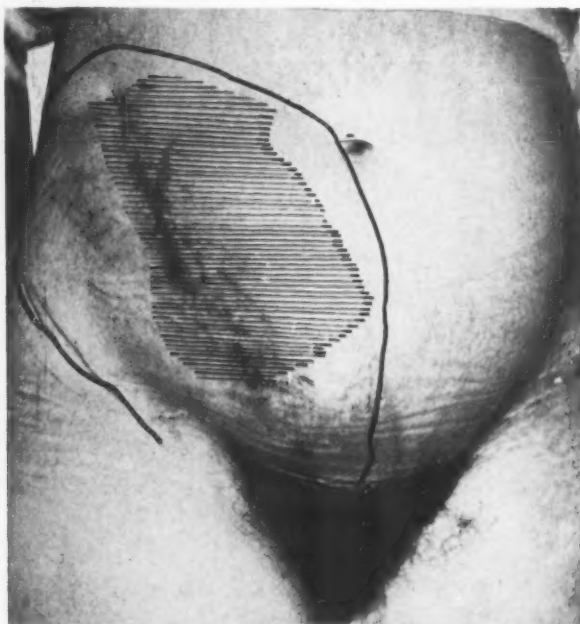


FIG. 6.—Case 2: M. Y. Photograph of abdominal wall a year and a half after extensive excision of musculature, fascia and neoplasm (sarcoma) of lower right quadrant, together with right colon adherent to under surface. An elliptical portion of the skin was also excised. Outline on skin indicates the approximate extent of musculo-fascial resection and in this area the abdominal parietes consisted of only skin and subcutaneous fatty tissue. Shaded area indicates approximate extent of peritoneal denudation at the time of the operation. Photograph taken at sixth month of pregnancy, and at this time there were bilateral pulmonary metastases, but the patient's general condition remained satisfactory.

COMMENT

That adhesions may occur following celiotomy, and that these may subsequently give rise to intestinal occlusion or be the cause of volvulus, needs no comment or elaboration. This is a long recognized fact. The cause of such adhesions, however, is probably not as readily explained as might be generally supposed, *i.e.*, on the basis of trauma to peritoneum, or defects in peritoneal surfaces, the healing of which leads to adhesive bands to underlying loops of bowel.

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It would appear that denuded parietal surfaces in the peritoneal cavity readily heal by proliferation of peritoneum at the margins of the area and/or by condensation of connective tissue in the denuded area to form a new smooth glistening surface membrane (peritoneum). It would appear that such reconstitution of peritoneal surfaces is the normal sequence and that this readily occurs unless other factors supervene. Among the latter may be mentioned infection, which stimulates fibrous tissue reaction and possibly interferes with the reappearance of the condensed superficial layer of tissue (peritoneum). Furthermore, there is the as yet undefinable tendency in some individuals to react to trauma by overproduction of fibrous tissue with dense collogenic interstitial substance.

The studies cited in the above report are not interpreted to indicate that complete disregard for reperitonealization is advocated. They are interpreted as suggesting that reperitonealization is not of sufficient importance to weigh heavily in determining the mode of procedure for radical extirpation of abdominal malignant neoplasms and that when reperitonealization of certain areas is not possible and is not carried out, this factor alone should be of no great concern in regard to possible subsequent development of adhesions which in turn may lead to angulation of bowel with occlusion or to volvulus of one type or another. Furthermore it may be inferred that after a complex and lengthy procedure, prolongation of the operation for meticulous approximation of the peritoneal layer in wound closure is not important enough to appreciably delay termination of the procedure and return of the patient to bed.

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DISCUSSION.—DR. HARVEY B. STONE, Baltimore: Mr. President and Members, I agree with the comments and the very interesting reports of Dr. Robbins and Dr. Brunschwig concerning excisions and removal of the parietal peritoneum. It has been my experience in excisions of the right side of the colon and of the left side of the colon that I was unable to do what I was directed to do by many authorities on this subject, namely, cover this defect by transplantation of peritoneum, because the defect extended often from the diaphragm to the brim of the pelvis and from the midflank line to the lateral margin of the vertebra, and in my hands, at least, there wasn't a possibility of covering the defect.

With considerable trepidation I permitted this raw space to remain for lack of anything to do about it, and discovered in a number of subsequent explorations of such abdomens that there was not, as the essayist has described, any extensive development of adhesions between the movable viscera and this denuded area, and that it had covered with a glistening surface which was to the naked eye undifferentiated from the rest of the peritoneum.

However, I think we must be careful in drawing inferences too broadly from what has been said. I would like to have in the published paper a little clearer distinction made between raw surfaces of a parietal nature and those of visceral nature.

Nothing in my experience—and, I must add, nothing in the experience as presented by the essayist—controverts the established principle that raw surfaces of gut and omentum are prone to develop dangerous adhesions with consequent obstructive conditions resulting, and that one must sharply distinguish between the importance of raw surfaces of parietal nature and of visceral nature, and that it is still imperative in good surgery to do what may be done to protect these raw surfaces of a visceral nature.

I should like to call attention to a recent article by Dr. Jere Lord and his associates in which he called attention to the Noble maneuver for plicating raw surfaces of peritoneum so as to self-cover the denuded surfaces. I believe that is a method which deserves much wider recognition than has been accorded it.

Mr. President, I am about to do something which I realize has no justification. I want to say that while I agree with what has been said about the significance and importance of raw surfaces of parietal peritoneum as related to these extensive operations, I would not like to be understood as agreeing that these operations in themselves are always desirable or defensible.

If I may extend the field of discussion a bit, I should like to call your attention to the fact that there is now a widespread tendency to extend tremendously the anatomical scope of attacks on cancer. There are certain things that I think we need to sharpen our thinking about in this regard.

In the first place, these procedures are not new methods of treating cancer; they are simply extensions of the accepted method, which consists of ablation of structures which are involved or may be involved in cancer. It is the best way we have at present for treating cancer, and our best is a very poor best. We must admit that. This new extension of the accepted principle of destruction is in no sense a new attack on the cure of cancer.

We are asked to extend these procedures to a degree which approaches what the economist speaks of as the point of diminishing returns, even though it be accepted that there is a salvage, a small percentage salvage, among the victims, shall I say, of these extensive operations. One has to weigh against that salvage the loss of function, the mutilation and the deterioration of health which often results. It is a question of balancing the possible advantages of salvages of these procedures against the increased mortality and increased morbidity and increased mutilation.

An analogy was made yesterday in one of the talks between the search for the last residual node and the attempt of a bird dog to go through a barbed wire fence to get a bird. I would like to suggest that the occasional bird which is recovered perhaps would not compensate the farmer for the destruction of the fence.

I think it might be well for us to balance these things carefully, and, shall I say, conservatively (that is a terrible word to use) before we commit ourselves too generally to this type of surgery.

DR. OWEN H. WANGENSTEEN, Minneapolis, Minn.: Mr. Chairman and Gentlemen, we have all listened with much interest to the presentation by Drs. Brunschwig and Robbins. They put the larger emphasis on the question of intestinal obstruction. That obviously is a matter of some importance—but I would think the larger question of importance would be how the absence of wide areas of peritoneum influences the healing of intestinal anastomoses.

A number of years ago, when we were toying with the elective primary intestinal resection in strangulated intussusceptions, Dr. W. P. Ritchie and I extraperitonealized an anastomosis which we had made in an infant, not being certain that it would be a good thing to leave it in the peritoneal cavity. We had planned to drop the anastomosis back into the peritoneal cavity. About the fourth day, however, Dr. Ritchie discovered a leak in it. Another of my associates, Dr. R. E. Buirge, then in the Experimental Surgical Laboratory, made a number of extraperitoneal as well as extracutaneous

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anastomoses, leaving the blood supply intact. These anastomoses all leaked. I believe the peritoneum affords an anastomosis some protection against leakage. I am not talking about the loss of peritoneum after hemicolectomy. My reference is to instances in which peritoneum is excised over large areas—operations in which the greater portion of the posterior parietal peritoneum to the lower abdomen and pelvis is sacrificed in the excision of large adherent cancers in the lower abdomen, and cases in which intestinal anastomoses are made in that area.

I have the feeling that one may leave such an operation with a greater sense of security with reference to the healing of single or multiple intestinal anastomoses if there is peritoneum there. I would like to ask Drs. Brunschwig and Robbins if they have had occasion to feel that extensive deperitonealization vitiated the healing of intestinal anastomoses made in the immediate vicinity of the deperitonealized areas.

For a number of years in patients upon whom I have found it necessary to excise large areas of peritoneum in the pelvis in the presence of concomitant intestinal anastomoses, I have employed a loop of the terminal ileum and its mesentery to reperitonealize the pelvis and to construct a new pelvic peritoneal floor. In concomitant excision of the uterus and pelvic organs, when the rectum is amputated in its mid-portion, such a loop can be applied against the posterior aspect of the coloproctostomy. This maneuver applies a supporting tissue to that anastomosis, at the same time it provides a means of reperitonealizing the posterior portion of the abdominal wall after sacrifice of its peritoneum. One can take this loop, suture it here and there, fan the mesentery out, and make an entero-anastomosis proximal to the cecum. This loop empties itself and covers the whole denuded area very nicely; moreover, it affords protection against leaks to any juxtapositional intestinal anastomoses.

All of us know that a dry wound is essential to healing, whether it be in a tooth socket, the pleura, the abdominal wall, or in the peritoneal cavity. If an anastomosis hangs suspended in a free space, unsupported by pliable tissues, it is not going to heal very well. I do not believe we should discount protection to intestinal anastomoses of adjacent peritoneum.

There are three operations which many of us do frequently, in which we do not rely too much upon available serous surfaces. One is a thoracic esophageal anastomosis. However, if we can mobilize pleura or the pulmonary ligament to cover the anastomosis, we feel better about it. The second is the Finsterer antral exclusion operation. The third is an extra or subperitoneal anastomosis of the rectum. Yet, in all these procedures, if we can cover or support the anastomosis with an available serous surface, I believe all of us feel that there is less risk of a leak in the anastomosis.

Now, I would like to speak briefly about this matter of a more radical operation. It is true, as Dr. Stone stated, that the salvage in late cancer is small. You will remember the Biblical admonition concerning the interest of the shepherd in the one sheep that had gone astray. Banks offer us one per cent on our money. Our discussion concerns the most valuable thing that people have—their lives. Until we are able to diagnose cancer early, we shall have to continue to manifest an aggressive surgical attitude toward cancer. There is no other satisfactory treatment in the majority of instances. And the salvage, even in late cases, is far greater than the one per cent current interest rate on money.

Until we have specific organ diagnostic technics or acceptable biologic tests for cancer, surgeons must continue to stress the importance of Cancer Detection Centers in the early recognition of cancer. Cancer is frequent; it is merely a question of: (1) Who will have it? (2) When? and, (3) In what organ?

I cannot agree with Dr. Stone that we should retrench rather than continue to pursue an aggressive attitude toward late cancer. To be sure, most of our efforts in late cancer are palliative. In gastric cancer in which the local lesion is excised, and in which hepatic metastases are present, the expected mean survival is 20 months in

our clinic. I have asked many a man if he has considered that reprieve worth while. The answer has always been in the affirmative. In this Voyage of Life, who expects to reach the other shore? We are all condemned to death; it is only a question of how long execution of the sentence may be delayed. Since man was driven out of the Garden of Eden, no one expects to live forever. It is our responsibility to make lives longer and happier if we can. Even old people who have been operated upon for cancer, in my experience, want to keep their frail vessels in this Voyage of Life afloat just as long as the voyage and the weather are pleasant.

There is an extension of operation in abdominal cancer which my colleagues and I have begun to explore, viz.: re-entry of the abdomen after a period of four to six months in Group C lesions (patients with lymph node metastases) to do a wiping-out operation. As yet, our experience is not large. But why wait 15 to 20 months for the reassertion of symptoms? That is the usual length of the silent interval in cancer.

The impress of surgeons upon the cancer problem is beginning to be felt. We must not lose heart; we must go ahead. We surgeons must continue a live interest in the cancer problem until help is available to us from other sources. When surgeons have the opportunity to operate largely on Group A or Stage I cancers, the late results of cancer surgery will begin to compare favorably with the results of surgery for benign conditions.

DR. JONATHAN E. RHODES, Philadelphia: I would like to refer briefly to some experiments on the formation of adhesions which Dr. Chandy, Dr. Portnoff, Dr. Jackson and I carried out in rats. We found not only that parietal peritoneum would regenerate but also that visceral peritoneum, if removed delicately and without injury to the deeper layers, would regenerate very well also.

If a fine silk suture was placed under the peritoneum of the rat and not tied, it would usually be sealed over without the production of an adhesion. However, when fine silk sutures were placed and tied, so as to oversew superficially denuded areas on the cecum, adhesions were frequently encountered. In fact, they were more frequent than when such areas were not oversewn but allowed to heal spontaneously.

One cannot apply conclusions from animal experiments to clinical practice without substantiating experience yet, in view of Dr. Brunschwig and Dr. Robbins' observations on the parietal peritoneum of patients, the problem of managing superficial injuries to visceral peritoneum in man should at least be reinvestigated. It may be that reperitonealization in patients would occur spontaneously with less adhesion formation than when sutures are used.

DR. JOHN C. BURCH, Nashville: It is perhaps unfortunate that the magnitude of Dr. Brunschwig's palliative operations has drawn attention from a more fundamental aspect of his work. I refer to his attack upon cancer of the cervix. At the present time this disease is killing about 25 out of every thousand women. By his broadening of the operation it is certainly possible that curative surgery can be attempted in certain cases now considered inoperable and palliative treatment can be achieved in an even larger number. For this I think Dr. Brunschwig is to be congratulated.

DR. ALEXANDER BRUNSCHWIG, New York City: I want to thank those who discussed our paper for their remarks.

The point raised, which I think was very well taken, was that we are talking about parietal peritoneum and not visceral peritoneum.

The reference to the Noble procedure is pertinent. It is an operation that should be carried out perhaps more often than it is when conditions indicate it.

As long as Dr. Stone has raised a question concerning radical resections in general, I want to make a statement or two, but I do not wish to prolong this into a

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discussion that could last for perhaps an hour, and besides it is not pertinent to our paper.

I think his words of warning are timely since radical excisions of advanced cancer are not to be undertaken lightly. About four years after Billroth first described gastrectomy, Welch, the late great pathologist at Hopkins, wrote a paper enumerating seven or eight reasons why gastrectomy was bound to be a futile procedure, pointing out that surgeons would never encompass gastric cancer by surgery and intimating that surgeons were indeed presumptuous in trying to do so. For almost every extension of surgery the same arguments can and have been raised.

In 1895 Nicholas Senn stated in his book on "Tumors" that he thought surgeons had gone too far in attacking cancer of the pylorus because he had operated on 16 and they had not survived, obviously due to the very poor supportive treatment available at the time.

For patients who have large cancers in the abdomen there is only one chance for prolongation of life and that is to get the tumors out. Whether one wants to take the chance, I think, is up to the individual surgeon in his attitude toward operating for cancer—some may be defeatists, others not. Some of you know that we reported 100 consecutive cases of so-called inoperable cancer, in a monograph.* I can report now the long-range results:

Thirteen of those patients, or 13 per cent, are living and well for over six years—after operation. They are not derelicts, they are not vegetables, but they have returned to useful, active lives.

Thirteen per cent is not a great salvage rate. This does not include an additional 6 per cent who survived an average of over three years and returned to normal useful lives. I should like to emphasize again that this is a series of patients that were selected for their *poor condition* rather than their favorable condition for surgical attack. If we consider *all* patients with gastric cancer that walk across the threshold of any clinic, I doubt whether we can be sure that we can salvage 13 per cent for six years, and among these would be a fair number of so-called favorable cases. In the series of 100 patients that I just alluded to, there was not a single "favorable case" and among them are included patients who had been explored elsewhere with nothing done because the situations encountered conformed to the classical criteria of inoperability.

* Radical Surgery in Advanced Abdominal Cancer. University of Chicago Press, 1947.

INTESTINAL OBSTRUCTION IN THE NEWBORN*

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IMPRESSIVE STRIDES have been recorded in intestinal surgery during the past quarter of a century, due to improved diagnostic aids, decompression of dilated intestinal loops by intubation, control of infection, more effective supportive therapy, and somewhat better operative technic. During the same interval the chance of survival of the newborn infant with intestinal obstruction has increased, but not to a degree comparable with the improved prognosis of the adult.

Twenty years ago only a few cases of intestinal obstruction in the newborn due to anomalies had been successfully treated. Just ten years ago Dr. Edwin M. Miller¹ reviewed the subject before the Association and reported several successful cases. In the discussion of Dr. Miller's paper, Dr. William E. Ladd reported 24 recoveries out of 29 cases of extrinsic obstruction and eight recoveries out of 17 cases of intrinsic obstruction from the Boston Children's Hospital. The best published figures to date are those of Ladd,² who in 1943 recorded 59 cases of extrinsic obstruction with 37 recoveries, and 87 cases of intrinsic obstruction with 23 recoveries. It would be impossible to overestimate the influence of the Boston Children's group upon the surgery of infants and children during the past three decades.

Within the past ten years a number of cases successfully operated upon have been reported by Arnheim,³ Biggs and Pontius,⁴ Bush et al,⁵ Donovan,⁶ Duncan et al,⁷ Duckett,⁸ Erb and Smith,⁹ Gomez and Lozoya,¹⁰ Judd,¹¹ Lyons and Brenazzi,¹² Martin,¹³ Medearis,¹⁴ Miller et al,¹⁵ Potts,¹⁶ Thompson,¹⁷ Wike,¹⁸ and Wright.¹⁹

That recoveries are no longer rarities does not, however, minimize the fact that the mortality of intestinal obstruction in the newborn remains high. Since means of decreasing mortality now seem available, a critical analysis of our failures, with a view to developing a more systematic approach to the problem, particularly from the standpoint of the surgeon, would appear to be of value. The series of cases presented by the authors shows mortality figures which are far from impressive. The patients were cared for by a number of surgeons in three large general hospitals. Analysis of the cases forms the basis for the observations and recommendations of the authors.

The most pertinent causes of mortality in the infant with intestinal obstruction are the following:

1. Many of the babies with intestinal anomalies are born prematurely and are poor candidates for any sort of operative procedure. The coincidence of

* Read before the American Surgical Association, St. Louis, Mo., April 21, 1949.

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other anomalies in these infants is also high. As surgeons we can offer little help to improve this factor. The prevention of premature births by the obstetrician and the internist may significantly alter these figures in the future.

2. *Delayed operation*, due to inaccurate or *tardy diagnosis*. This is probably the most important preventable factor in the high mortality. Many of these delays are chargeable to the obstetrician or the pediatrician but many are due to indecision on the part of the surgeon. The improved mortality that goes with earlier recognition and earlier operation is demonstrated in the tables presented.

3. *Inadequate supportive therapy* is probably the next factor of

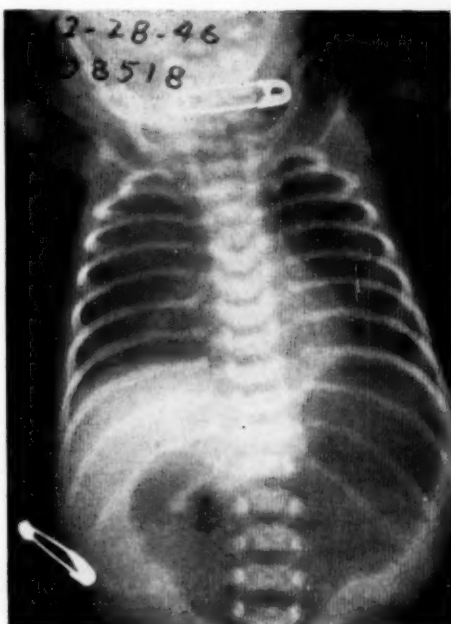


FIG. 1.—Case 6. Typical gas shadow of the dilated stomach and duodenum of complete atresia of the duodenum proximal to the ampulla of Vater.

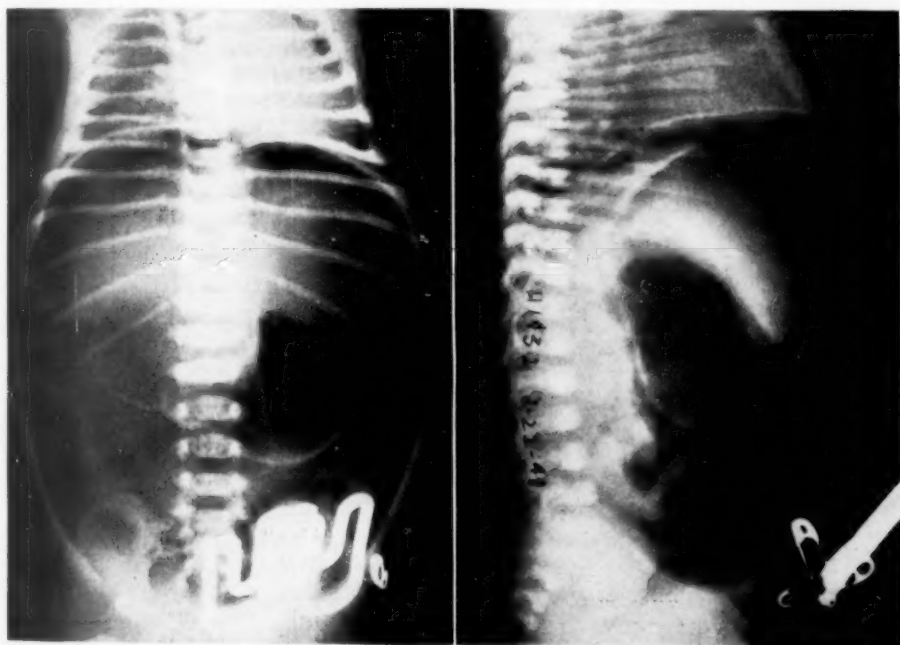


FIG. 2.—Case 3. Atresia of duodenum proximal to the ampulla with perforation and pneumoperitoneum. The roentgenograms show the distended stomach and duodenum as though suspended in gas within the peritoneal cavity. The collapsed small and large intestines can be seen. No contrast media necessary.

importance. Shock and peritonitis have, in the past, contributed heavily to the mortality.

4. *Operative indecision* and unphysiologic operative measures are about as important as inadequate supportive therapy in contributing to the mortality.

DIAGNOSIS

Early diagnosis merits special emphasis. Vomiting in the newborn infant is too common to cause concern but when the vomitus contains bile and when the abdomen is distended on the first day of life, the diagnosis should be considered to be intestinal obstruction due to an anomaly until proved to the contrary. The acceptance of this simple, didactic statement literally would save many lives. Very few babies who vomit soon after birth due to functional

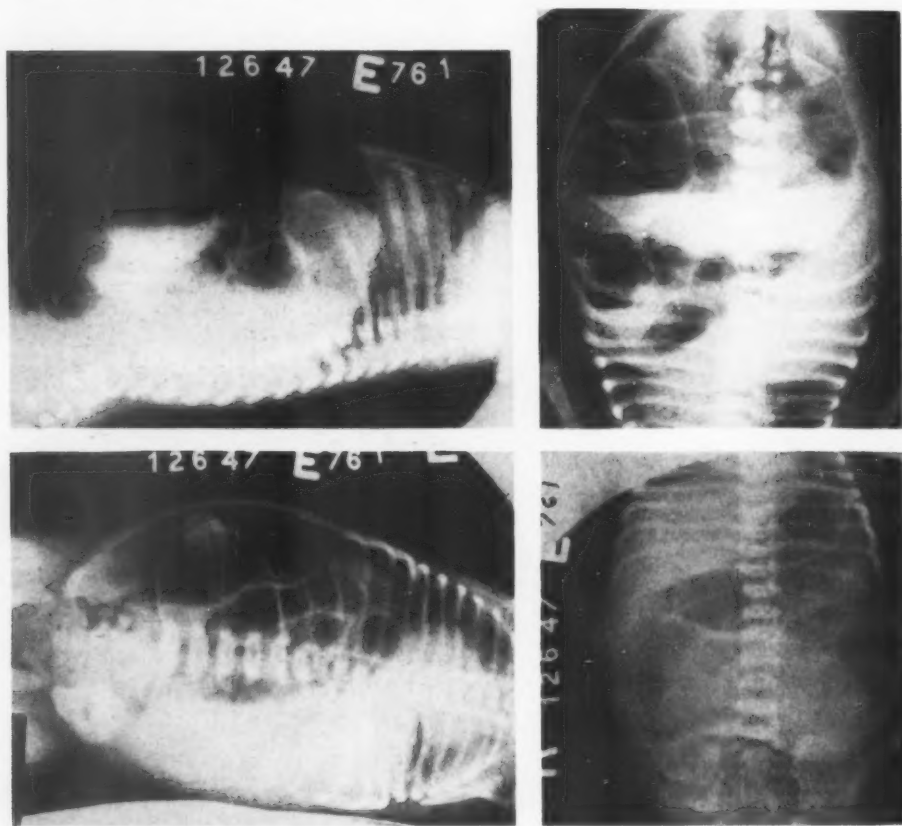


FIG. 3.—Case 17. Ileal atresia with perforation. Plain roentgenograms in four different positions show multiple distended and gas-filled loops of small intestine, fluid levels within the loops and also free in the peritoneal cavity, and pneumoperitoneum.

causes show abdominal distention. When the abdomen is tightly distended, furthermore, with tympany that obliterates liver dullness, with shiny skin and dilated superficial veins, the diagnosis of intestinal obstruction with perforation, pneumoperitoneum and peritonitis is almost certain. Symmetrical distention of the abdomen, in the absence of pneumoperitoneum, usually implies

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obstruction in the jejunum or ileum. Distention of the upper abdomen alone implies duodenal obstruction. Visible peristalsis is often apparent, coursing from left to right over the upper abdomen, especially when obstruction is in the duodenum or upper jejunum. The absence of bile in the vomitus does not rule out obstruction, since the point of atresia or stenosis may be proximal to the ampulla of Vater. Visible peristalsis is likely to be present in such cases. The presence of visible peristalsis within a few days after birth almost always indicates the presence of congenital obstruction in the upper intestinal tract. Pyloric stenosis occurs so rarely at this age as to be statistically insignificant.

The vomiting of meconium-like material is usually indicative of a duodenal obstruction. In case No. 3 the vomitus and the stool appeared almost identical. In several of our cases the vomitus contained gross blood. With the obstruction in the jejunum or ileum the vomitus is more likely to be of an intestinal character. The lack of milk curds in the stool of the newborn infant is also diagnostic evidence of importance. The stool of a normal infant on breast or formula begins to show some milk curds within the first 24 hours, or at the latest, on the second day of life. The absence of such findings may be considered evidence of complete obstruction. Farber's²⁰ test, showing the presence or absence of cornified squamous epithelial cells in the stool, may be of some help in determining the continuity of the intestinal tract, as is the absence of bile in the stool, but other criteria have seemed more certain to us.

Vomiting due to intrinsic obstruction occurs almost always during the first day of life and is continuous from that time on. If obstruction is due to extrinsic factors alone, however, vomiting may not start on the first day and it may be intermittent, and part of the feedings may be retained for days or even weeks after birth. (Cases Nos. 36, 7, 42.) In cases of extrinsic obstruction due to errors of rotation it is common to have the baby pass normal stools for several days, decreasing in amount as the degree of obstruction increases. If the obstruction is low in the colon, vomiting may not start for several days after birth. Except where obstruction is high in the duodenum, vomiting is not likely to be projectile.

In addition to the evidences already mentioned, the distended stomach and

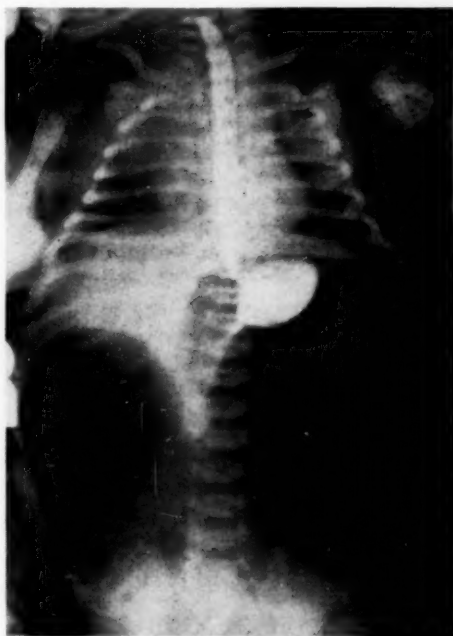


FIG. 4.—Case No. 45. Three-day-old infant with stenosis of the duodeno-jejunal junction. The duodenal gas shadow fills the entire abdomen. The stomach is small in size and contains only a little barium. This is a very unusual picture.

duodenum, or loops of ileum, usually can be palpated through the thin abdominal wall unless obscured by pneumoperitoneum or diffuse peritonitis.

The plain or "flat" roentgenogram of the abdomen is unquestionably the most helpful diagnostic aid in intestinal obstruction of the newborn that is available. It is usually possible to identify the gas-filled viscus and its location, with sufficient accuracy to provide approximate localization of the point of obstruction. The plain roentgenogram will almost always make the diagnosis of duodenal or intestinal atresia apparent. (Figs. Nos. 1, 2, 3, 5.) Information may be obtained from films taken in different position, and by injecting air into the stomach after evacuating the contained fluid.

When the diagnosis is quite clear from the clinical evidence and from the plain roentgenogram, the use of barium is to be avoided since its presence in the intestine may complicate the postoperative course. When the diagnosis is



FIG. 5

FIG. 5.—Case 18. Atresia of the distal ileum. The roentgenogram shows the distended loops of small intestine and also shows the colon to be in approximately normal position but of small caliber.



FIG. 6

FIG. 6.—Case 20. The roentgenogram shows marked distention of the entire colon due to stenosis of the sigmoid.

not complete without barium, however, its use is definitely indicated. The barium enema alone may be very helpful in identifying the approximate level of the atresia in the ileum (see Fig. 5), or to demonstrate the presence of a colon on the left side of the abdomen, in cases of malrotation (Fig. 7), or to distinguish between colon and distended ileum (Fig. 6). The diagnosis of extrinsic obstruction due to errors of rotation may not be possible from the plain roentgenograms alone and here a small amount of barium by mouth, with or without the addition of barium by rectum, may greatly simplify the diagnosis (Figs. 7, 8).

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In short, the history of vomiting bile soon after birth, together with abdominal distention and abdominal gas shadows in the plain roentgenogram, are usually sufficient to make a presumptive diagnosis of intestinal obstruction due to a congenital abnormality.

SUPPORTIVE THERAPY

It is axiomatic that the small infant tolerates blood loss, shock and dehydration poorly, and these factors are all operative in the newborn with intestinal obstruction. Our ability to give adequate quantities of whole blood to the babies, before, during, and after operation, together with the ability to control postoperative infection with antibiotics, has greatly widened the limits of operability.

It is to be assumed that the baby with congenital intestinal obstruction will have been maintained on parenteral fluids since birth. The newborn infant, if born at term, will tolerate two or three days of starvation and moderate dehydration, but many infants with anomalies are born prematurely and for

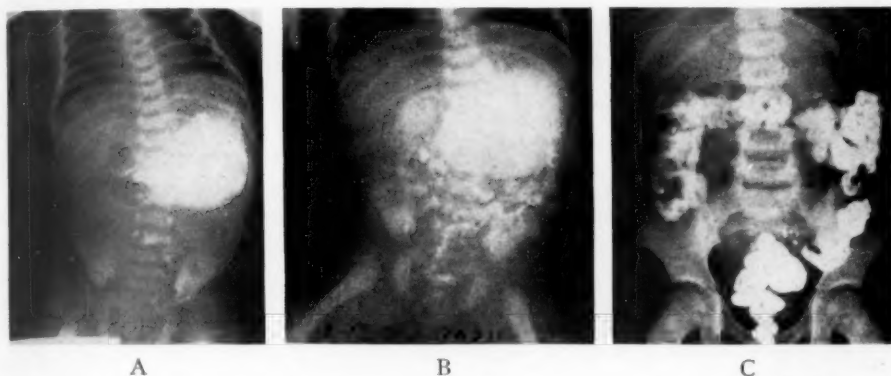


FIG. 7.—Case 29. Malrotation and volvulus. A. shows the typical picture with barium in the dilated stomach and a gas-filled duodenum, with only a few flecks of gas below. B. shows that a few flecks of barium have passed into the jejunum. Barium enema given at the same time shows a diminutive colon entirely on the left side, a fact which practically clinches the diagnosis. C. shows the same child at six years of age. Barium enema shows the colon in normal position. In this case the cecum was placed upon the right side at operation.

them the period of starvation is a much more serious one. During the interval between the time a surgeon makes the diagnosis and the time of operation, as much parenteral physiologic fluid should be administered as will be absorbed. If the baby is obviously depleted, time will be well spent in giving a blood transfusion of 75 to 100 cc. of whole blood slowly, following with an equal amount of electrolyte solution. The surgeon should not make the incision in the abdomen until a needle is in a vein, or in the bone marrow, and blood is running satisfactorily, no matter how good the patient's condition may seem to be. Unless this absolute rule is followed, the surgeon may find himself engrossed in untangling the anomalous situation of the intestinal tract only to discover that the baby is in severe shock and the anesthetist and

assistants are unable to get blood started. It is advisable to leave the cannula or needle in the vein or bone marrow after operation and continue either blood or electrolyte solution as indicated, at a slow rate, for some hours after operation.

While it is felt that intravenous transfusion is generally preferable, technical considerations occasionally make bone marrow transfusions the method of choice, both during the operation and subsequently. Bone marrow infusions are not without danger (see Case No. 17) but offer the advantage of being able to use the same site for repeated injections. Whether or not permanent injury can be done to the bone marrow cavity of the long bones in this manner is still open to question. When the infant's life depends upon blood transfusion in a hurry the bone marrow route offers obvious advantages.

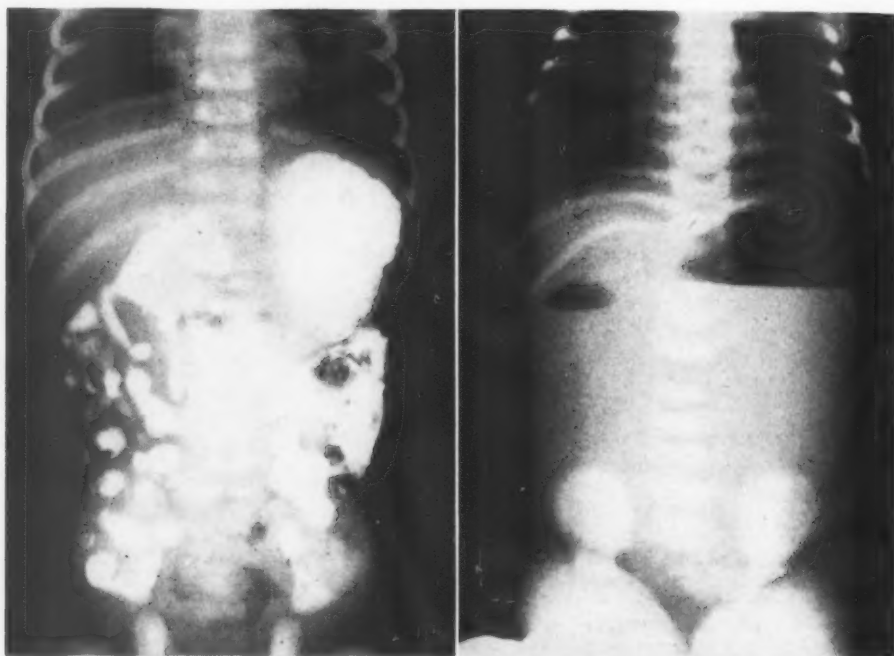


FIG. 8.—Cases 37 and 38. These two roentgenograms show the extremes of findings in cases of malrotation with volvulus. Case 37 on the left, who was operated upon at six days of age, shows considerable barium in the small intestine as well as dilated stomach and duodenum. Case 38 on the right was operated upon at two days of age, and on the plain roentgenogram shows the two large gas bubbles and fluid levels characteristic of duodenal obstruction, but no gas in the intestine. Both recovered.

After operation the problem of maintaining fluid and protein balance is often difficult, especially if fluid is being lost from a temporary enterostomy or by rectum due to a short-circuiting operation. Under such circumstances the management of replacement therapy becomes an exacting problem which requires the most careful supervision of the pediatrician and surgeon. Day

to day observations on the relation of intake to output, cytological and chemical blood examinations are required if serious depletion is to be avoided. The earlier that the needs of the infant can be met through protein-containing fluid absorbed from the intestinal tract, the less the danger of serious imbalance.

Penicillin seems to be the antibiotic of choice for routine use. We prefer to have penicillin given intravenously prior to and during the operation in order to maintain a good blood level when the peritoneum is opened. In cases of resection, anastomosis or other potential source of contamination of the peritoneum, penicillin is continued for several days. If there is at any time evidence that infection is not controlled by penicillin, or that the causative organism is penicillin-resistant, other antibiotics are used. Because of its low toxicity, penicillin seems to be most desirable for routine use in newborn infants.

OPERATIVE MANAGEMENT

Anesthesia, incision and extent of exploration. The junior author prefers ether anesthesia and a right rectus incision. The senior author prefers procaine ($\frac{1}{4}$ per cent) anesthesia and a transverse incision, upper right for duodenal lesions and lower right for lesions in the ileum or colon. We both feel however that the matters of anesthesia and incision are very personal ones with the operator and, particularly when operating on babies in precarious condition, the surgeon should use the method of approach with which he feels most comfortable. The combination of anesthesia and exposure which makes it possible for the surgeon to explore the abdomen thoroughly with minimal trauma and loss of time, and to do a definitive operation accurately, is the optimum. When a surgeon who is accustomed to working under general anesthesia attempts to use local anesthesia on a difficult case, he is likely to be handicapped and the patient is likely to suffer.

In the years before adequate supportive measures were available, we often attempted to correct the cause of obstruction through a small incision without thorough exploration. We now feel that such an approach is wrong. With the available methods of preventing and combatting shock and infection there are very few infants, whose condition justifies any attempt at operation at all, who cannot tolerate thorough exploration. We feel strongly now that the abdomen should be explored thoroughly regardless of the cause of the obstruction or its apparent ease of correction. The incidence of multiple causes of obstruction is high. (Cases 15, 31, 43, 44, 45.) Incomplete exploration ranks high as one of the causes of failure in our series, as well as in other reported cases.

Assessing the probabilities. The surgeon must be aware of certain fundamental facts and probabilities before he opens the abdomen; these may be summarized in simplified form as follows:

1. The common sites of atresia or stenosis are: (a) the second part of the duodenum, near the ampulla of Vater; (b) the duodenal-jejunal junction (which is also the site of obstruction due to congenital bands, retroperitoneal

hernia and volvulus due to malrotation); (c) the distal ileum; (d) the distal colon and rectum.

2. Ring pancreas alone may cause obstruction, but it is often accompanied by intrinsic obstruction of the duodenum (Cases 1, 7).

3. The majority of congenital obstructions of the duodenum are distal to the ampulla of Vater.

4. Incomplete rotation with partial or complete volvulus usually causes obstruction at or near the duodenal-jejunal junction.

5. Incomplete rotation often occurs concomitantly with atresia or stenosis of the duodenum or ileum. It is important to remember that release of the volvulus due to malrotation does not fulfill all the requirements for complete operation unless it is clearly demonstrated that no other obstruction exists by passage of a catheter or Levine tube through the duodenum into the jejunum.

6. The incidence of multiple points of obstruction is sufficiently great to demand thorough exploration in every case.

7. Defects in the mesentery, bands and points of irregular fusion of the peritoneal layers which are capable of causing obstruction often accompany malrotation (Cases 30, 42, 43, 44).

8. Marked dilatation of the colon occurs in the presence of atresia or stenosis of the distal colon (Case 20). This is a rare finding.

TECHNICAL CONSIDERATIONS

Operation is always performed with a small Levine tube or catheter (No. 8 or 10 French) in the stomach for the purpose of constant decompression. Before opening the peritoneum the surgeon has made a tentative diagnosis on the basis of the criteria previously mentioned, and the incision is planned accordingly. Upon opening the peritoneum, one or more of the following alternative findings will immediately present:

1. The presence of free gas and fluid in the peritoneum necessitates an immediate search for the point of perforation in order to avert further peritoneal contamination. The most likely point of perforation is the ileum and the next most frequent is the second part of the duodenum. If the small intestine is dilated it should be delivered immediately to control the point of perforation. If the small intestine is not dilated it may be assumed that the perforation is in the duodenum, and since there will be little danger of additional leakage, the stomach and duodenum having been deflated by the gastric tube, orderly exploration may proceed.

2. The position of the colon is at once noted. If the cecum is not in its customary position on the right side of the abdomen or is not visible at all, malrotation is at once suspected. If a mass of bluish purple loops of small intestine present immediately, either collapsed or containing only a small amount of gas, volvulus about a common mesentery is more than likely. The obstruction may or may not be due to the malrotation, however.

3. Distention of the stomach and duodenum alone implies that the point of obstruction is at or proximal to the ligament of Treitz.

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4. Dilatation of the small intestine and a small, collapsed colon, indicates that atresia or stenosis in the small intestine is probable.

5. Dilatation of the colon, as well as part of the small intestine, indicates a rare type of stenosis or atresia of the distal colon at or proximal to the sigmoid.

The next step is evisceration and systematic exploration of the abdominal contents.

Extrinsic duodenal obstruction. The incompletely rotated colon is dealt with first. It is necessary to follow a deliberate and systematic course of procedure if confusion is to be avoided, for when the bowel is pulled this way and that in an attempt to find the point of obstruction rapidly it is far too easy for the operator to become confused and miss the true point of obstruction. The next step is to divide the hepatocolic ligament, free any lateral attachments to the cecum and the superior peritoneal attachments of the right half of the transverse colon which will usually overlies the transverse portion of the duodenum. This exposes the entire length of the duodenum to the ligament of Treitz and permits placing the entire colon on the left side of the abdomen. If the colon is in fetal position, never having rotated at all, and having formed no attachments on the right side, this step is unnecessary. If there is a volvulus of the entire small intestine which has rotated about the superior mesenteric artery, usually clock-wise, this is now replaced by untwisting the bowel and the mesentery until the latter is unobstructed and the jejunum follows a straight course from the ligament of Treitz (Figs. 9, 10 and 11). The peritoneal attachments of the duodenum, laterally and inferiorly, are now freed up to and including the folds of peritoneum which comprise the ligament of Treitz, using great care not to injure the superior mesenteric artery which is carefully examined for abnormal bands or folds which may surround it. The duodeno-jejunal junction now lies to the right of the superior mesenteric artery and the duodenum empties vertically into the jejunum. One of the maneuvers just described will probably relieve the obstruction of the duodenum if it is due to the volvulus about the common mesentery, or abnormal attachments about the ligament of Treitz or the superior mesenteric artery. The exploration must not be discontinued at this point, however. The duodenum, which has been exposed, is carefully examined. If obstruction was present in the third portion of the duodenum, it will be elongated as well as dilated. The gastric tube or catheter is then passed through the duodenum into the jejunum. If it meets no obstruction, and passes readily into the jejunum, the operator may be assured that no obstruction remains up to that point. Gas is then followed through the entire small and large intestine to make certain of the patency of the remainder of the intestinal tract.

The procedure just described and illustrated was advocated by Ladd²¹ in 1932, and has been given credit for the striking improvement in cures of extrinsic obstruction of the duodenum.

Intrinsic duodenal obstruction. If the stomach and duodenum remain dis-

tended and the catheter meets an obstruction in the second or third parts of the duodenum, the surgeon is faced with alternative possibilities: (1) to do an anastomosis between the proximal duodenum and the jejunum or between

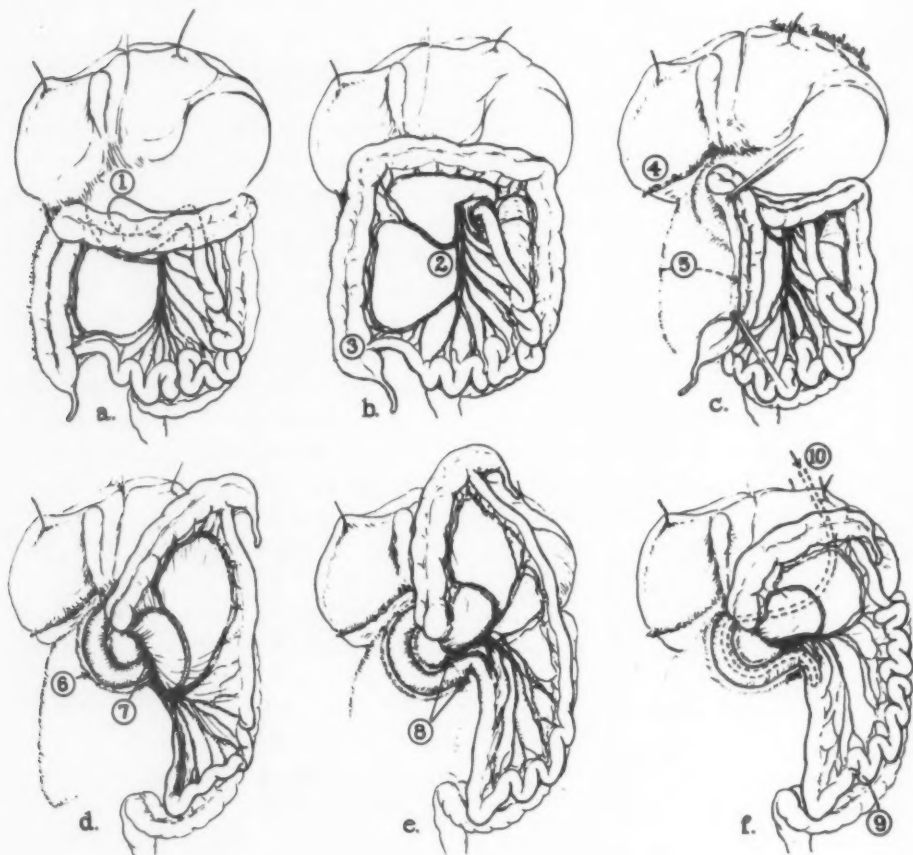


FIG. 9.—This series of diagrams represents the steps that we feel necessary for the complete exploration of the duodenum in order to properly evaluate the degree of obstruction that may be present. The operation must be done under adequate anesthesia and through an ample incision.

Step 1.—Examination of the pylorus to rule out pyloric stenosis.

Step 2.—Examination of the base of the mesentery.

Step 3.—Examination of the cecum to determine the degree of rotation of the large intestine, to rule out volvulus of the small intestine.

Step 4.—Cutting of the hepato-colic ligament to free the hepatic flexure of the colon.

Step 5.—Cutting of the secondary attachments of the ascending colon to completely visualize the duodenum.

Steps 6 and 7.—Cutting of the secondary attachments of the duodenum to the abdominal wall and the secondary attachments to the base of the mesentery of the small intestines at the superior mesenteric vessels. This does not interfere with the blood supply of the duodenum.

Step 8.—Complete freeing of the secondary attachments of the duodenum at the ligament of Treitz to allow the duodenum to descend on the right side of the abdomen.

Step 9.—Demonstration of the passage of gas into the small intestine.

Step 10.—Passage of a Levine tube into the small intestine to rule out the presence of partial septa within the duodenum.

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the stomach and jejunum; or (2) to open the intestine at the point of obstruction in the hope of finding a leaflet which can be resected without anastomosis. If the stomach and proximal duodenum are markedly thinned out and lacking in tone due to distention of long standing, an anastomosis is probably the safer procedure since, even if the leaflet is removed, it will be a matter of days before the atonic stomach and duodenum are able to force fluid through the collapsed loops. If, however, the tone seems good and distention is not excessive, the procedure described by Morton²² and illustrated in Figures 9 and 10 may be useful. The bowel is incised longitudinally over the point of obstruction, and if a leaflet is found obstructing the lumen of the duodenum, it is resected, the mucosa carefully repaired, and the bowel wall closed in its transverse diameter. The catheter is then passed through the anastomosis.

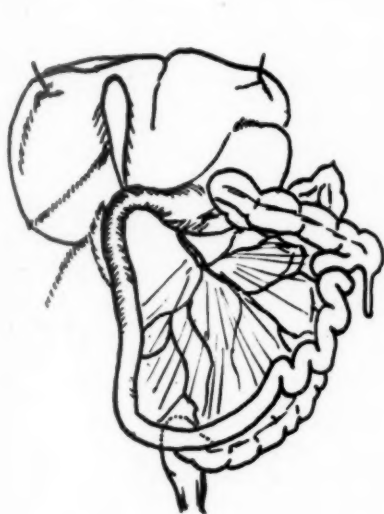


FIG. 10

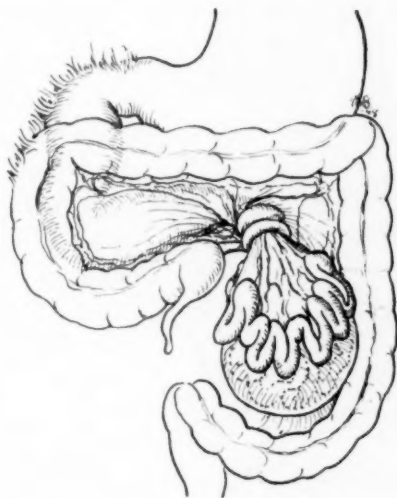


FIG. 11

FIG. 10.—This is the final position in which the duodenum should be left, if possible, in all cases of malrotation of the colon with obstruction of the duodenum. With the duodenum descending on the right side of the abdomen and the colon on the left, the base of the mesentery is no longer a small point of fixation but becomes a wide base and postoperative recurrent volvulus should not occur.

FIG. 11.—Case 30.—A complete 360 degree volvulus of the small intestine in a counter-clockwise direction was found. The case illustrates the fact that the duodenum may be dilated in this situation. It is not always. There was also herniation of a portion of the terminal ileum into its own mesentery, which is shown as a pouch that includes the volvulus. The colon was more completely rotated in this case than is usual in the presence of volvulus.

If, instead of the findings just described, there is obvious loss of continuity of the duodenum, either near the ampulla of Vater or near the duodeno-jejunal junction, an anastomosis is obviously the only choice. A duodeno-jejunosomy is generally preferred. If, however, the duodenum has been very

markedly distended, the wall thinned out, a gastro-jejunostomy through the thicker walled stomach may be somewhat safer. While a posterior anastomosis is preferable, an anterior anastomosis is perfectly satisfactory if it is easier to do. Our choice is for a lateral isoperistaltic duodeno-jejunostomy performed with two rows of 5-0 silk on atraumatic needles. No clamps are used, the thumbs and forefingers of the assistant serving as admirable holders which are much less traumatizing than clamps. The gastric catheter or Levine tube may now be passed through the anastomosis into the jejunum for a distance of 15 to 20 cm. to insure its patency, and the anesthetist may inject slowly, 5 or 10 ccs. of saline through the catheter into the jejunum. More saline may be introduced slowly through the catheter from time to time while the operation is being completed. This procedure aids in dilating and straightening out the loops of small bowel, helps the surgeon to be assured that continuity of the bowel exists, and at the same time provides the infant

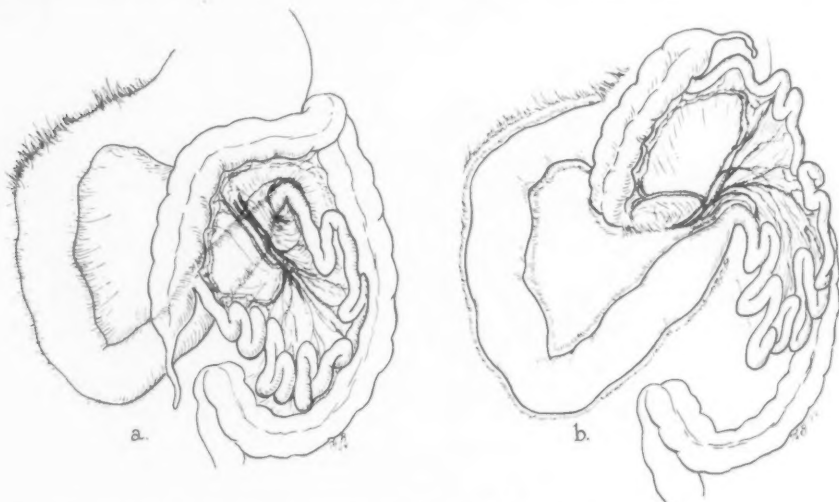


FIG. 12.—Case 34 (a.) A typical instance of incomplete rotation and fixation of the colon with obstruction of the duodenum at the ligament of Treitz. Note the marked dilation and particularly the elongation of the duodenum which forces it completely out from under the colon. The surgeon often gains the impression upon first examination that the duodenum actually passes through the mesentery of the terminal ileum.

(b.) By carefully dissecting the ascending colon free, it is possible to free the duodenum completely at the ligament of Treitz; by freeing the secondary attachments the duodenum can be brought down into the right lower abdomen, thus preventing recurrent postoperative volvulus by widening the base of the mesentery.

with badly needed electrolyte fluid. If there is a great discrepancy between the size of the duodenum and the collapsed jejunum, the latter may be dilated with saline prior to the anastomosis as an aid to suturing.²³ This is not usually necessary, however.

When obstructions of the duodenum have been relieved, especially those due to atresia of some days' standing, and where the muscle-tone of the former organs is lacking, it is absolutely essential to keep the stomach con-

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tinuously deflated in order to protect the integrity of the suture line of the anastomosis. It is also highly advantageous to be able to begin introducing feedings into the jejunum immediately after the operation. The presence of an indwelling catheter or tube is not well tolerated by the nasopharynx of the small infant, and favors aspiration. It is unsafe to leave the tube in place for more than a day or two continuously. The tube introduced through the nasopharynx does not, furthermore, serve effectively as a deflating mechanism, if it has been passed through into the jejunum; and if it is left in the stomach



FIG. 13

FIG. 13.—Case 10. A typical case of complete obstruction of the second part of the duodenum due to an imperforate septum. External adhesions were thought to be the cause of obstruction until it was discovered that the Levine tube would not pass, illustrating the importance of completing the steps of the exploration, as advised in the text.

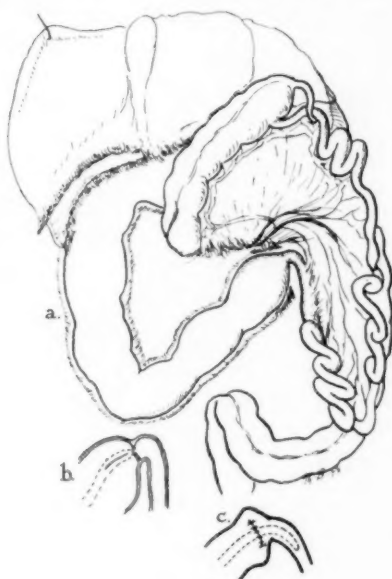


FIG. 14

FIG. 14.—Case 11. The findings illustrate the not uncommon instance of two or more causes of duodenal obstruction in the same patient. Roentgenograms showed that the opaque material had passed the point of obstruction, which exploration proved to be at the ligament of Treitz. When an attempt was made to pass the Levine tube, a partial septum was found near the duodeno-jejunal junction. The use of a simple plastic procedure for removal of the septum, as shown in the illustration, is possible only if the duodenum is freed completely. Otherwise a duodeno-jejunostomy must be performed.

it is impossible to use it for feeding. The tragic results which may follow failure to keep the stomach deflated are illustrated by Case No. 3, where the anastomosis leaked.

The amount of air swallowed by the small infant during crying and gulping is astonishing. We have measured as much as 10 to 15 ccs. of air swallowed per gulp while the baby was crying. It is easy to see that this amount will soon dilate the stomach and jejunum to a point where leakage at the anastomosis line is almost inevitable.

To overcome this objection we have introduced two small catheters through the stomach wall (Fig. 16). The end of one catheter is passed through the anastomosis into the jejunum to serve as a feeding tube, while the other catheter remains in the stomach for maintaining continuous suction until the suture-line has had an opportunity to heal. The catheters are anchored securely to the stomach wall with fine silk sutures and also to the abdominal wall and are securely strapped to the abdominal wall with adhesive tape to avoid inadvertent removal. Through the feeding tube fluid can be introduced into the jejunum by slow drip, and within a day or so the infant's nutritional requirements can be met through this source.



FIG. 15

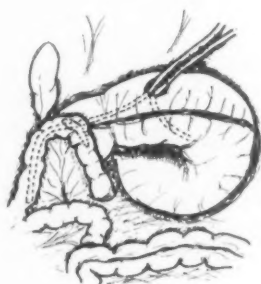


FIG. 16

FIG. 15.—Case 3. Atresia of the duodenum proximal to the ampulla of Vater.

FIG. 16.—Case 3. A posterior duodeno-jejunostomy has been performed. Two small catheters have been placed through the gastric wall, one through the anastomosis to serve as a feeding tube and the other left in the stomach to aspirate swallowed air.

Final position of the colon. While it has been asserted by Ladd that the colon must remain on the left side of the abdomen after the operation is completed in order to safeguard against subsequent intestinal obstruction, the senior author has on occasion deliberately placed the cecum and ascending colon on the right side of the abdomen, without any fixation whatever, and has left them in that final position. Roentgenogram (Fig. 7) following barium enema six years after the operation on such a case shows the cecum and ascending colon to have remained in the normal position. It is interesting to note that gastro-intestinal series showed the duodeno-jejunal junction to have remained in vertical position on the right side of the abdomen, emptying in a perfectly normal manner. We have occasionally observed evidences that after birth the process of rotation of the colon, which was arrested during fetal life, may continue. This observation lends support to the procedure of leaving the colon in a position where it can continue rotation after birth and perhaps form normal attachments. This maneuver must be done with great caution, however, and if the bowel does not lie perfectly free over the small

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intestine without twisting or kinking the mesentery, it is far safer to leave it on the left side in the fetal position.

Other rare causes of obstruction which may be encountered are ring pancreas (Cases 1, 7), retroperitoneal hernia (Cases 31, 34), intramesenteric hernia (Case 30), and volvulus about remnants of the omphalo-mesenteric duct (Case 36).

Intrinsic obstruction of jejunum and ileum. Since atresias of the small intestine are often multiple (Cases 15, 26) it is obviously most important to establish continuity with as much length of both small and large bowel as can be salvaged. Where the point of atresia or stenosis is single, a side-to-side anastomosis may be done quickly between the loops proximal and distal to the occlusion without disturbing the blind ends. If, however, the points of atresia are multiple it is usual to find a very short distal loop of ileum at the



FIG. 17

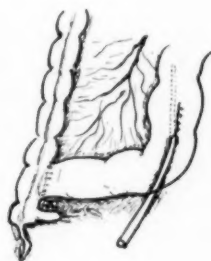


FIG. 18

FIG. 17.—Case 17. Ileal atresia with perforation of the blind end of ileum. Two tiny segments of rudimentary intestine may be seen between the blind loop and the ileocecal valve.

FIG. 18.—Case 17. An end-to-side ileo-colostomy has been performed after resecting the distended blind loop and the rudimentary segments shown in Figure 17.

ileocecal valve and it is necessary to do an anastomosis between the markedly dilated proximal loop of ileum or jejunum and the colon, which is usually so small as to make the anastomosis difficult. Here an end-to-side anastomosis is probably best. A Witzel-type enterostomy tube should always be left in the dilated proximal loop to control distention until the anastomosis functions (Fig. 18). Whether or not to leave the blind loops of ileum in place is a question that is usually determined by expediency. If they are so small as to be worthless, they may as well be resected, if the procedure will not add unreasonable operative trauma. If the blind loop is of more than 20 cms. length, however, it is well to leave it, on the chance that if the baby survives it may prove useful later. It is most important to make certain of the patency of the diminutive colon which is occasionally occluded by a cast-

like cord of cells (Case No. 16). A useful expedient is to introduce the tip of the enterostomy catheter (before completing the Witzel closure) through the anastomosis into the colon, and through this to introduce saline which can be milked along the colon to insure its patency and continuity. The colon may also be dilated from below by repeatedly introducing fluid through the rectum.

It is sometimes tempting to do an anastomosis between the dilated ileum and the sigmoid colon which looks slightly larger in calibre than the diminutive ascending and transverse colon (Case 17) but this should not be done because it permits the baby to lose fluid too rapidly to get ahead. Open ileostomies are to be condemned. The surgeon should use every possible effort to do a definitive operation that will make it possible for the infant to acquire his nutritional requirements through the intestinal tract at the earliest possible date. The time required to do an anastomosis is insignificant if the baby is receiving blood during the operation.

When the entire large bowel down to the descending colon or sigmoid is found to be enormously dilated, as well as part of the ileum, the point of obstruction will usually be found in the lower colon, but it may not be complete and the findings may be confusing (see Case No. 20). In such cases a catheter usually can be introduced through the rectum and fed through the narrow point unless the obstruction is complete enough to require resection and immediate anastomosis. In either case, a temporary tube cecostomy is worth-while to decompress the bowel until the stenotic area can be dilated.

Atresia of the rectum. Atresia of the rectum is usually readily diagnosed by the lack of an anal opening, failure to obtain meconium by probing the intact anal plate, and by plain roentgenograms taken in the head down position as suggested by Wangenstein.²⁴ The latter procedure forces gas in the blind end of the colon in the pelvis, usually near the bladder neck, where it can be easily seen. With this evidence, operation should always be performed through the perineum. By very careful, gentle dissection through a small incision, the blind end of bowel can usually be found in the region of the bladder neck and can be freed retroperitoneally, sufficiently to mobilize it and bring it down to the perineum. The bowel is opened and sutured to the skin, the sphincter being reconstructed at the same time. These procedures are highly successful and carry a very low mortality. Abdominal colostomy is almost never necessary in such cases and should be avoided.

CASE REPORTS; INTRINSIC OBSTRUCTION

Case 1.—The infant was born with several anomalies and was not operated upon. At autopsy complete atresia of the duodenum was found proximal to the ampulla of Vater. (Previously reported.²⁵)

Case 2.—A premature male infant weighing 3 pounds and 8 ounces was explored on the fourth day of life. Markedly distended stomach and duodenum were found. The patient stopped breathing several times during the procedure, which was terminated without attempt to relieve the obstruction. The baby died two days later. Autopsy showed incomplete stenosis of the second part of the duodenum and a perforated ulcer of the ileum. A patent ductus arteriosus and a patent foramen ovale were also present.

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Case 3.—A male premature infant weighing 5 pounds was observed to vomit all feedings from the time of birth, the vomitus resembling meconium. A small amount of meconium was also passed per rectum. The vomitus contained no bile. When seen 24 hours after birth, the infant's abdomen was tensely distended throughout, liver dullness was obliterated and the skin was shiny, with mottling and venous engorgement. Plain roentgenograms showed marked distention of the stomach and proximal duodenum with no gas visible elsewhere in the intestinal tract. A large amount of free air was present in the peritoneum (Fig. 2). At operation 36 hours after birth atresia of the duodenum proximal to the ampulla of Vater was demonstrated. The cecum was in fetal position on the left side of the abdomen. The perforation could not be identified since the stomach and duodenum had been evacuated through a No. 10 catheter passed into the stomach, but was assumed to be in the first part of the duodenum where distention had thinned the wall greatly. An isoperistaltic duodeno-jejunostomy was performed with 5-0 silk in three layers, and the catheter was passed through the stoma into the distal limb of the jejunum for feeding purposes. The baby was given whole blood followed by Ringer's solution by bone marrow infusion during and after the operation. The baby's condition was excellent the following day and small feedings were begun through the tube. On the second day he passed several milk stools mixed with meconium. It was necessary to place an additional catheter in the stomach to decompress the air the baby swallowed constantly. On the fifth day it was apparent that the baby again had pneumoperitoneum. Assuming that the anastomosis had leaked, the incision was reopened and that fact confirmed. The anastomosis was repaired and two small catheters were introduced through the stomach wall, one going through the anastomosis to serve as a feeding tube and the other to keep the stomach decompressed. The baby died the next day apparently of shock and bile peritonitis.

Case 4.—The full term infant began vomiting soon after birth, but retained part of its feedings, and during this admission evidence of obstruction was unrecognized. At ten months of age he was readmitted with a history of intermittent vomiting since birth and failure to gain weight, and died within a few minutes of admission. Autopsy showed incomplete stenosis due to a leaflet in the second part of the duodenum proximal to the ampulla. (Previously reported.²⁵)

Case 5.—The infant was operated on at six days of age and lysis of adhesions performed in the region of the ampulla where obstruction seemed to exist. The baby died eight days later from what was presumed to have been an intrinsic stenotic lesion just distal to the ampulla. (Previously reported.²⁵)

Case 6.—A $2\frac{1}{2}$ -pound premature female infant whose vomiting from the time of birth was projectile and bile-stained was admitted about eight hours after birth. Marked visible peristalsis was noted from left to right in the upper abdomen and the roentgenogram showed a typical picture of duodenal obstruction. Under local anesthesia and with bone marrow transfusion running, exploration showed the infant to have a ring pancreas. After dividing the encircling ring of pancreas, however, it was found that a catheter could not be passed through the duodenum at this point due to complete stenosis. A duodeno-jejunostomy was accordingly performed and the catheter passed through the anastomosis. The baby passed milk stool on the second day but succumbed on the fourth day.

Case 7.—A five-weeks'-old infant was admitted with a history of vomiting bile-stained material intermittently and increasingly in amount, weight loss and dehydration. There was marked visible peristalsis, and roentgenograms showed dilatation of the stomach and proximal duodenum. Exploration showed a ring pancreas to be the apparent cause of obstruction. This was divided. Because of continued vomiting the baby was reoperated upon four days later. Since it was apparent that an intrinsic stenosis existed distal to

the ampulla, an anterior gastro-jejunostomy was performed. The baby recovered without incident and has remained well for 12 years. (Previously reported.²⁵)

Case 8.—The newborn infant was observed for ten days prior to death, but not operated upon. In spite of the fact that roentgenograms had showed that barium passed freely into the small intestine, at autopsy esophagus, stomach and duodenum were enormously distended due to intrinsic stenosis at the duodeno-jejunal junction. (Previously reported.²⁵)

Case 9.—A six-weeks'-old infant was explored for pyloric stenosis which was not found. At autopsy a few days later partial stenosis at the duodeno-jejunal junction was demonstrated. The infant also had other anomalies. (Previously reported.²⁵)

Case 10.—A female infant was admitted two days following delivery, with a history of vomiting bile-stained material on the first day. On the second day of life the vomitus contained coffee ground material. The stool contained only meconium. Examination showed the upper abdomen to be distended after feedings, with peristaltic waves running from left to right, and flat roentgenograms showed the gas-filled stomach and duodenum. Upon exploration, rotation of the colon was found to be complete. The first and second part of the duodenum were dilated and elongated. The transverse portion of the duodenum was normal and the Levine tube would not pass into this portion (Fig. 13). The duodenum was opened longitudinally across the point of constriction and a complete septum was found at that point. The septum was excised and the incision was closed transversely. Recovery was uneventful and the child has remained in normal health for seven years.

Case 11.—A ten-day-old infant was admitted with a history of intermittent vomiting since birth, but for the few days prior to admission all of each feeding was vomited, and the vomitus contained bile but no blood. Stools were scanty but normal in color. Examination showed upper abdominal distention after feedings, with visible peristalsis. Roentgenograms with barium showed an enlarged and elongated duodenum with almost complete obstruction at the ligament of Treitz. Very small amounts of air and barium passed into the small intestine. Three days after admission the abdomen was explored. The duodenum was tremendously enlarged and elongated. At the ligament of Treitz were a kink and a band which were freed, but the Levine tube still failed to pass that point. The duodenum was opened at that point and a septum was found, in the center of which was a slit-like valvular opening 4 mm. in length (Fig. 14). The septum was excised and the incision in the bowel was closed transversely. Roentgenograms 17 days later showed marked improvement but not return to normal. The patient has remained well for two years since operation.

Case 12.—The patient was operated upon on the day of birth. The distal 2 feet of ileum were represented by a small band about which was twisted the blind end of ileum, the latter being gangrenous. An ileostomy was done and the baby died 24 hours later. (Previously reported.²⁵)

Case 13.—This baby presented a picture similar to Case No. 12 when operated upon on his third day of life, and he died following ileostomy. (Previously reported.²⁵)

Case 14.—This female infant, explored on the first day of life, was found to have a stenosis of the distal ileum with marked dilatation of the proximal ileum and jejunum. A resection and side-to-side anastomosis was performed. Vomiting and abdominal distention continued intermittently and when two weeks later the abdomen was reexplored a supplementary lateral anastomosis was performed between the proximal ileum which still remained dilated and the ascending colon. Her condition was improved following this procedure but she did not gain well, and had intermittent bouts of abdominal distention suggesting partial obstruction. In spite of adequate supportive therapy she developed pneumonia and died four weeks after the initial operation. Autopsy showed no other

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evidence of intestinal anomaly, but the baby had a patent ductus arteriosus and a patent septal defect.

Case 15.—A female infant weighing approximately 5 pounds was admitted 48 hours after birth with a history of vomiting all feedings, with marked distention of the upper abdomen, visible peristalsis and roentgenographic evidence of marked distention of the stomach and entire duodenum. A side-to-side anastomosis was performed between the third part of the duodenum and the distal ileum. In spite of supportive therapy the infant died the following day. Autopsy showed seven points of atresia between the ligament of Treitz and the ileocecal valve. (Previously reported in detail.²⁰)

Case 16.—This male infant was admitted to the hospital eight days after birth with a history of vomiting intermittently since birth and only one meconium stool passed on the fourth day of life. In spite of the vomiting the infant had taken feedings well. At first the vomitus was bile-stained but subsequently became fecal in character. An enema on the day of admission brought returns of greenish mucus. Roentgenograms showed a typical picture of obstruction of the distal ileum. At operation upon the day after admission, atresia was found in the distal ileum, with marked dilatation of the entire intestine proximal to the point of obstruction. An end-to-end ileostomy was performed after resecting the dilated distal loop and distending the distal ileum with saline to increase its size. On the seventh postoperative day the anastomosis perforated and the baby died of peritonitis. Terminally the infant was edematous, probably due to administration of an excess amount of parenteral fluid. Autopsy showed the distal loop of ileum and the ascending colon to be almost occluded by a cord-like mass of cellular debris which had prevented the functioning of the anastomosis. Patient also had patent ductus arteriosus, patent foramen ovale and portal thrombosis.

Case 17.—A premature female infant seen on the third day of life had begun vomiting on the first day and on the day prior to examination had vomited all feedings. The vomitus contained bile. The abdomen was uniformly distended, with drum-like tympany throughout, the skin being stretched so that the superficial veins were easily visible. Liver dullness was obliterated. Baby had passed a little meconium on the first day but nothing subsequently. Roentgenograms showed enormous distention of several loops of small intestine as well as free fluid and gas in the peritoneal cavity (Fig. 3). Operation was performed on the third day of life, under local anesthesia, through a lower transverse incision while blood was given via bone marrow. The peritoneal cavity contained a large amount of free gas and a moderate amount of greenish fluid. It was found that the enormously distended ileum ended in a blind loop which was fixed in the pelvis and had perforated, and that there were two tiny segments of rudimentary bowel about 1 cm. by 4 mm. in diameter between this point and the ileocecal valve (Fig. 17). Colon was in normal position but only about 5 mm. in diameter. The distended distal ileum had twisted upon itself in such a manner as to produce virtually a closed loop approximately 4 cm. in diameter by 10 cm. in length. This loop contained thick liquid material and gas and the wall was almost gangrenous. This loop was resected and a lateral anastomosis was performed between the ileum and the sigmoid colon, which seemed to be the only part of the colon large enough to be likely to function effectively, and an ileostomy tube was placed in the distal end of the ileum. The infant took feedings well, passed stools from the rectum immediately following the operation and fluid balance was maintained by parenteral electrolyte solution and intramarrow transfusions of whole blood and plasma. Frequent stools continued from the rectum but drainage from the ileostomy gradually increased in amount until at the end of three weeks it was apparent that the patient was losing fluid more rapidly than could be compensated for. Accordingly, at this time the ileostomy was resected and an end-to-side anastomosis was performed between the distal ileum and the ascending colon which had now increased in size until it was about 1 cm. in diameter. After this procedure the infant began to improve rapidly but still required some parenteral

feedings. She died suddenly following an intramarrow plasma infusion at the age of four weeks. While fat embolus from too rapid introduction of the plasma was suspected as the cause of death, this could not be confirmed at autopsy. No other anomalies were disclosed.

Case 18.—This male infant of 5 pounds, 14 ounces at birth, began vomiting immediately after birth and was suspected of having an intracranial lesion for the first three days. It was apparent on the third day, however, that the baby had a complete intestinal obstruction. Operation was performed on the fourth day disclosing an atresia of the distal ileum and a lateral ileo-transverse colostomy was performed. The baby was in poor condition at the time of the operation and the anastomosis never functioned. He died on the first postoperative day. No autopsy was obtained, but there seems to be some question if the colon was actually patent distal to the anastomosis in this case.

Case 19.—This infant was operated upon the third day of life, presenting an atresia of the entire colon down to the distal sigmoid. The baby died following ileosigmoidostomy. (Previously reported.²⁵)

Case 20.—This male infant of normal size began to show abdominal distention soon after birth and on the third day began to vomit. Roentgenograms (Fig. 6) showed marked distention of all intestinal loops and barium introduced per rectum showed marked distention of the entire colon down to the sigmoid. At operation, performed on the fourth day of life, no point of obstruction was found. Autopsy performed 24 hours later showed incomplete stenosis to exist in the midportion of the sigmoid colon. Patient also had a patent ductus arteriosus and a patent foramen ovale.

Case 21.—This 18-hour-old term female infant showed abdominal distention from birth, vomited bile and passed no stool. Roentgen examination showed marked distention of the stomach and duodenum and what was interpreted as gas in the colon, thought to be due to an enema. She was transfused and operated upon under drop ether anesthesia and found to have an atresia of the terminal ileum with a wedge shape defect in the mesentery and a collapsed portion of ileum below that point. A lateral anastomosis between the dilated and collapsed loops of ileum was done, and the child recovered. She was later admitted with a diagnosis of fibrocystic disease of the pancreas. She is the sibling of Case 46 who had a meconium ileus and fibrocystic disease of the pancreas.

Case 22.—This one-day-old term female infant was operated upon on the first day of life under drop ether anesthesia because of abdominal distention and absence of stool. Roentgenograms showed dilatation of the greater portion of the small intestines. There was found to be complete atresia of the terminal portion of the ileum, a wedge shaped defect in the mesentery and a collapsed distal loop of ileum. A lateral anastomosis was performed between the distal and proximal loops, but the child died after eight hours.

Case 23.—This one-day-old term male infant vomited and became distended from the time of birth, and the vomitus contained bile. Roentgen examination showed dilatation of the greater portion of the small intestine. He was transfused and explored under drop ether anesthesia and found to have a complete atresia of the terminal ileum with a wedge-shaped defect in the mesentery. An end-to-end ileo-cecostomy was done, with survival.

Case 24.—This two-day-old term male infant was seen because of vomiting of bile and distention of the abdomen since birth and a roentgenogram showing dilatation of the greater portion of the small intestines. He had a complete situs inversus. He was transfused and explored under drop ether anesthesia and found to have an abdominal situs inversus with the exception of the large intestines. There was a reverse rotation of the colon so that the duodenum which was on the left side descended directly into the jejunum and was not retroperitoneal at all. The colon lay with the cecum in the right lower quadrant but it passed up and behind the small intestines instead of in front of it and was a retroperitoneal organ. There was a complete defect in the terminal ileum, with

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several small cystic remnants of ileum in the terminal portion and a collapsed terminal ileum about three inches in length. An ileo-cecostomy was performed. This functioned postoperatively, but only poorly, because there was a continuing partial obstruction in the colon where it passed behind the superior mesenteric vessels and the dilated jejunum. An ileostomy was done above the anastomosis 11 days after the original operation in an attempt to decompress it, but in spite of this the child died 27 days later. In retrospect it would seem that something should have been done to prevent the obstruction in the transverse colon, either by doing the anastomosis to the left half of the transverse colon, or of transecting the colon and reanastomosing it in front of the vessels.

Case 25.—This three-day-old term female infant was noted to refuse all feedings from birth, and to vomit bile. The abdomen became distended and peristalsis was visible. No roentgen examination was made. She was transfused and operated upon under drop ether anesthesia and found to have a diaphragm across the terminal ileum 8 inches above the ileocecal valve. A plastic operation was done on the valve, excising it and closing the gut. At the time of the operation it was felt that there was some question about the viability of the intestines adjacent to the septum. The child died after 8 hours, from peritonitis. Postmortem examination also showed incomplete expansion of the lungs.

Case 26.—This three-day-old term male infant was noted to have had no stools and to vomit, the vomitus containing bile. A barium enema was done, and the colon filled only to the splenic flexure and there was tremendous dilatation of the small intestines. The child was transfused and operated upon under drop ether anesthesia. There was a focal area of marked enlargement of the jejunum and multiple areas distal to that in the ileum and colon in which there was no apparent lumen of the intestines. Interposed were segments of apparently normal intestine. These were interpreted as multiple areas of complete atresia and nothing was done. The child died after six days and at autopsy the area of dilated jejunum previously described was again noted, and although the remaining portion of the intestinal tract had a lumen it was reduced in size. The apparent cause of death was peritonitis.

CASE REPORTS; EXTRINSIC OBSTRUCTIONS

Case 27.—This five-day-old infant had vomited bile or bile-stained fluid since birth. Examination revealed distention and visible peristalsis in the upper abdomen; stools were brown and soft with curds. Roentgenograms with opaque material revealed the stomach and duodenum to be widely dilated, and what little opaque material entered the jejunum was on the right side of the abdomen. A few gas shadows on the left suggested colon. The history and roentgen findings were considered typical of partial duodenal obstruction due to malrotation and volvulus. At operation, the cecum was found to be in the upper abdomen overlying the duodenum and there was a 360 degree clockwise volvulus of the entire small intestine. There was also partial obstruction of the first part of the jejunum where it went through a defect in the mesentery, and it was further fixed by the peritoneal attachments of the cecum. The latter were freed, and the volvulus reduced. The attachments of the duodenum were not freed. Recovery was uneventful, and the patient has remained well for ten years. (Previously reported.²⁵)

Case 28.—A five-weeks'-old infant presented a picture of high intestinal obstruction, and upon exploration disclosed a partially rotated colon with stenosis of the second part of the duodenum due to the peritoneal attachments of the unrotated cecum. Freeing these permitted filling of the third part of the duodenum and jejunum. The attachments of the duodenum and cecum were not otherwise disturbed. The baby's recovery was uneventful. (Previously reported.²⁵)

Case 29.—A healthy appearing infant of almost 8 pounds at birth, began vomiting the first day after birth and continued to vomit with increasing frequency until seen by

the pediatrician and surgeon on the seventh day. The vomitus contained bile. The baby passed meconium on the first day, a few small yellow or brown stools on the second and fifth days, and had no stools on the sixth and seventh days. When seen he was dehydrated and showed upper abdominal distention with marked visible peristalsis. Roentgenograms taken following ingestion of barium showed marked dilatation of the stomach and duodenum and only a few flecks of barium in the small intestine. Barium injected by rectum showed the colon to be entirely on the left side (Fig. 7.) The diagnosis of malrotation with volvulus was confirmed at operation. Reduction of the volvulus did not relieve the duodenal obstruction, however, because it was constricted near the ligament of Treitz by peritoneal bands. Release of the attachments of the cecum and transverse colon and duodenum permitted the duodenum to empty freely. Without disturbing the root of the mesentery, the cecum was carefully rotated to the right lower quadrant of the abdomen and left there without fixation. Recovery was uneventful. The child has remained free from symptoms for eight years. Roentgenograms following barium enema taken six years after operation showed the entire colon to occupy the normal position (Fig. 7). The duodenum emptied vertically into the jejunum on the right side of the abdomen.

Case 30.—E. W., a 2900 Gm. premature male infant had been in the hospital since birth. Although his development had been slow, he seemed to be progressing normally except for intermittent vomiting. On the 40th day following delivery, he began to vomit everything that he took by mouth. The vomitus occasionally contained blood. Physical examination revealed an underdeveloped and dehydrated infant. The upper abdomen was distended and there were visible peristaltic waves passing from left to right across the upper abdomen. Roentgenological examination revealed a gas bubble in the stomach and another in the duodenum, and a uniform ground-glass appearance of the lower abdomen. The child was transfused and explored through a right rectus incision under drop ether anesthesia. On examination of the ligament of Treitz, there was found to be a complete 360 degree volvulus of the entire small intestine in a counter-clockwise direction. The cecum was completely rotated, but the distal ileum disappeared through what appeared to be the orifice of an internal hernia. As the volvulus was reduced, it was found to completely obstruct the duodenum at the ligament of Treitz. The duodenum proximal to that point was elongated and dilated. As the mesentery was straightened out, there was found to be a secondary obstruction due to the herniation of the terminal ileum into a sac formed by an outpocketing of a fold of mesentery between two vascular arcades. About 8 inches of intestine were in this sac (Fig. 11). The hernia was reduced, and the sac obliterated by suturing its mouth. The colon was mobilized, the duodenum completely freed and explored, and a tube passed through it. The colon was allowed to fall back to the left side of the abdomen and was not reattached. The child's postoperative course was uneventful and he was discharged 2 weeks later. The patient was readmitted 2 weeks later with another bout of intestinal obstruction. He was explored and secondary adhesions in the terminal ileum were found to be the cause of obstruction. His recovery was uneventful.

Case 31.—B. W., a four-day-old colored boy was admitted to Babies' and Children's Hospital following a normal delivery with a history of vomiting almost all feedings since birth. Vomiting followed feedings by 20 to 30 minutes, and the vomitus contained bile. The stools contained meconium, and on one occasion appeared normal. Roentgenologic examination revealed dilatation of the stomach, air in the duodenum, and almost none in the small intestine. The child was explored under drop ether anesthesia on the fourth day of life. The cecum was found in the right upper quadrant. The first, second and third portions of the duodenum were enlarged. On examination of the ligament of Treitz, a herniation of the first part of the jejunum into a retroperitoneal sac adjacent to the ligament of Treitz was found. This was the cause of obstruction, and when it was reduced, air passed freely. The sac was obliterated, and the

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abdominal wall closed, leaving the intestine in place. The child did not do well, and continued to vomit. Repeated roentgenologic examination showed that some gas passed into the small bowel, but very little. On the sixth postoperative day, the child was explored a second time. The neck of the previous hernia was closed, but there was a complete 270 degree volvulus of the entire small intestine with the ligament of Treitz and colon as an axis. The volvulus was reduced, and the hepatocolic ligament divided. The lateral peritoneal reflection of the right colon was incised, and the duodenum completely freed and explored with a Levine tube. The colon was allowed to drop back into the left side of the abdominal cavity. The child's recovery was complicated by continued vomiting of parts of each feeding for several weeks. The child continued to lose weight for 6 weeks, but at that time vomiting diminished, and he began to gain weight. His eventual recovery was complete.

Case 32.—The newborn infant was observed for eight days while vomiting and distention increased. At operative exploration the entire small intestine and the large intestine up to the splenic flexure were described by the operator as dilated. No error of rotation was noted. The baby died following ileostomy and no autopsy was obtained. It seems possible that this was a case of reversed rotation. (Previously reported.²⁵)

Case 33.—The newborn infant was operated upon with a diagnosis of pyloric stenosis, but obstruction was found to be due to a defect in the gastro-colic omentum through which a loop of jejunum had herniated into the omental bursa. Recovery followed replacement of the bowel and closure of the defect. (Previously reported.²⁵)

Case 34.—J. P., a seven-day-old white girl was born October 19, 1947, following a normal pregnancy and spontaneous delivery. She was fed within 12 hours, and vomited immediately. She was offered several formulae, but never retained more than half of a 30 cc. feeding. On the day before admission, she vomited everything despite atropinization to the limit of tolerance. The infant had been maintained on parenteral fluids. Physical examination revealed a normal, healthy female infant. Following each feeding the upper abdomen was greatly distended with fluid and air, and peristaltic waves were visible passing from left to right. Vomiting was immediate and projectile; the vomitus contained bile. The stools were meager and light brown. Roentgenologic examination on October 23, 1947, revealed a large amount of air in the stomach and duodenum, and a moderate amount in the small intestine. Barium studies showed an obstruction in the third portion of the duodenum beyond which only very small flecks of barium passed. Under drop ether anesthesia, the duodenum was explored. The rotation and fixation of the intestine were normal. The first and second portions of the duodenum were dilated and elongated. On freeing the third portion of the duodenum, the superior mesenteric artery was found in a tight fold of peritoneum which constricted the portion of duodenum which passed beneath it (Fig. 12). The entire duodenum and colon were mobilized. Postoperatively the child was fed 5 per cent Karo within 12 hours, and protein SMA after 24 hours. She continued to vomit small amounts of some feedings in decreasing amounts for 6 days, although the vomiting was never projectile and peristaltic waves were never visible. After the first week, recovery was uneventful.

Case 35.—R. V., a five-day-old white girl was admitted to the Babies' and Children's Hospital with a history of vomiting all feedings since birth, in spite of dietary modifications and atropinization. Pregnancy was normal, and delivery by low forceps uncomplicated. She vomited the first and subsequent feedings completely. The vomitus contained bile, and after 48 hours, flecks of blood. The stools were scant but contained bile. Physical examination was normal. Roentgenologic examination revealed air in the stomach, first, and second portions of the duodenum, and a small amount of air in

the small intestine. Injection of 60 cc. of air through the Levine tube into the stomach accentuated the radiographic picture. The child was explored on the fifth day of life under drop ether anesthesia. The intestines were normally rotated. The proximal duodenum was dilated and elongated up to the ligament of Treitz, where there was a definitely tight peritoneal band. When this was freed, gas passed freely into the jejunum and a Levine tube passed easily. The child's convalescence was slow. She continued to vomit 5 to 10 cc. of each 60 cc. feeding for ten days. At the time of discharge, vomiting had ceased and the stools were normal.

Case 36.—This ten-week-old normal term male infant developed severe vomiting and progressive abdominal distention, and was admitted to the hospital 40 hours after the onset of symptoms. He was severely dehydrated. The abdomen was quiet. Roentgen examination showed dilatation of the entire small intestine with a typical ladder pattern. After blood and electrolyte balance were restored, his abdomen was explored under drop ether anesthesia. A Meckel's diverticulum existed with a cord extending from its tip to the ileo-cecal valve and the intervening gut was caught under this cord, twisted and gangrenous. The gangrenous segment was resected and an ileo-cecostomy done, with survival.

Case 37.—This six-day-old term male infant vomited most of his feedings from birth. The vomitus contained bile and the stools were scant. Roentgenograms showed distention of the stomach and duodenum and barium studies showed partial retention of barium in the stomach after 24 hours. He was transfused and the abdomen explored under drop ether anesthesia. An incomplete attachment of the colon with a 360° clockwise volvulus of the entire small intestine on the ligament of Treitz was found. The volvulus was reduced, the duodenum freed and left on the right side of the abdomen, and the colon on the left. The child recovered and had no further vomiting.

Case 38.—This two-day-old premature male infant was seen because of persistent vomiting of bile-stained material, no stools, and distention of the upper abdomen. Roentgenograms showed a dilated stomach and duodenum, and no air in the rest of the intestinal tract. He was transfused and operated upon under drop ether anesthesia and found to have incomplete rotation and fixation of the colon with a 360° volvulus, counterclockwise, of the entire small intestine. This was reduced and the duodenum completely freed and returned to the right side of the abdomen, the colon to the left. The child had some vomiting postoperatively for ten days. Since then the child has developed normally.

Case 39.—This 18-day-old term male infant's abdomen was explored under drop ether anesthesia after 15 days of conservative treatment for persistent vomiting of bile-stained material, upper abdominal distention, visible peristalsis and scanty stools. He was found to have a 360° volvulus of the entire small intestine at the ligament of Treitz with incomplete obstruction of the duodenum. The volvulus was reduced and nothing else done. The child survived and developed normally.

Case 40.—This three-day-old, six weeks premature, male infant had vomited bile-stained material since birth. Roentgen examination showed some air in the intestinal tract and a suggestion of fluid between the loops of intestine, indicative of peritonitis. He was operated upon under drop ether anesthesia and found to have an incomplete rotation of the colon with a 720° counterclockwise volvulus of the entire small intestine. The small intestine was gangrenous so that nothing could be done, and the child died in three hours.

Case 41.—This three-day-old term male infant was admitted because of vomiting of bile-stained material since birth. Roentgenograms showed a dilated stomach and

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duodenum and absence of air in the small intestines. Exploration done under drop ether anesthesia showed an obstruction at the ligament of Treitz, presumably due to extrinsic bands, but the duodenum was not freed. A duodeno-jejunostomy was done and the child survived and developed normally.

Case 42.—This two-and-one-half-months-old female infant was admitted because of failure to gain weight, vomiting of bile-stained material, visible peristalsis from left to right in the upper abdomen and barium retention in the stomach after six hours. She was operated upon under drop ether anesthesia and found to have an enlarged stomach and duodenum with obstruction that was interpreted as extrinsic at the ligament of Treitz. A duodeno-jejunostomy was done and the child died of peritonitis on the fifth postoperative day. Autopsy demonstrated a partial stenosis in addition to the extrinsic fold, which caused partial obstruction at the duodeno-jejunal junction.

Case 43.—This six-week-old premature male Mongolian idiot had had vomiting of bile-stained material since birth. The upper abdomen was distended and the stool scanty. Roentgen-ray examination showed tremendous dilatation of the stomach and duodenum and no air in the small intestine. He was operated upon under local anesthesia and found to have an incomplete rotation of the colon with obstruction of the duodenum at the ligament of Treitz due to extrinsic peritoneal folds. These were freed and the child was better for 2 days but again began to vomit, and died on the sixth postoperative day. Autopsy showed, in addition to the extrinsic obstruction, a partial septum at the ampulla of Vater.

Case 44.—This six-day-old female term infant had had jaundice since birth and vomited all feedings, the vomitus containing bile. There was visible distention of the upper abdomen and peristalsis from left to right. Stools were absent. She was operated upon and found to have extrinsic obstruction around the second portion of the duodenum due to bands, which were freed. The patient died 13 days postoperatively. Autopsy revealed, in addition to the extrinsic obstruction, a partial septum at the ampulla of Vater.

Case 45.—This three-day-old term male infant vomited bile and all feedings from birth. The upper abdomen was distended and he had no stools. Roentgenograms showed a tremendous double loop of duodenum and a small stomach. He was operated upon and an extrinsic obstruction at the ligament of Treitz, incised freeing the duodenum. He did not improve and on his tenth postoperative day was reoperated upon and the duodenum was freed more completely. He continued to vomit, and died six days later. The surgeon interpreted this case as one of primary megaloduodenum.

Case 46.—This two-day-old term female infant was admitted because of distention of the abdomen and small stools containing only meconium. Roentgenograms showed distention of the small intestines. She was operated on under drop ether anesthesia and found to have two areas in the small intestines in which the gut was herniated into its own mesentery, requiring a double resection of the small intestine and lateral anastomosis. The child died after five days, of peritonitis.

Case 47.—This one-day-old term male infant vomited bile from birth and showed marked abdominal distention. Roentgen examination showed distention of the entire small intestine, the stomach and duodenum. He was operated upon under drop ether anesthesia and the jejunum and a portion of the ileum were markedly dilated. Beginning in the mid-portion of the ileum there was an abrupt diminution in the size of the gut to a cord like structure which contained inspissated meconium. This was broken up and partially passed into the colon by massage and the injection of saline through a fine needle. On the operating table the child had two large meconium stools. He died 24 hours later. The autopsy showed that the lumen of the intestines was patent but that the abrupt change in the size of the gut persisted. The child also had fibrocystic disease of the pancreas.

COMMENT

The small series of cases reported does not lend itself to complete statistical analysis. The figures presented in the tables may, however, justify certain generalizations. It seems apparent that the extrinsic obstructions represented by errors of rotation, carry a distinctly lower mortality rate than do the intrinsic defects, chiefly because they are incomplete. The atresias carry a much higher mortality rate because they represent complete obstructions, and also because they are frequently accompanied by associated anomalies, chiefly cardiac.

TABLE I.—*Mortality*

Type of Obstruction	Authors' Series	Cases	Deaths	Mortality
Extrinsic.....		16	4	25%
Extrinsic and intrinsic.....		4	3	75%
Intrinsic.....		24	18	75%
Totals.....		44	25	57%
Ladd's Series ²¹				
Extrinsic.....		59	22	37%
Intrinsic.....		87	64	73%
Totals.....		146	86	59%

In this report we have not attempted to separate the intestinal atresias from the stenoses, since the classification is difficult at best, and the only functional difference between the two is in the relative degree of obstruction produced. The stenotic lesions along with the errors of rotation carry a lower mortality rate than the complete atresias, as reflected in Table IV.

TABLE II.—*Intrinsic Defects*

	Cases	Deaths	Mortality
Duodenal.....	8	5	62%
Duodenal and extrinsic.....	4	3	75%
Ileal.....	14	11	78%
Colon.....	2	2	100%
Totals.....	24	18	75%

It has been generally assumed in the literature that the duodenal atresias offer a better prognosis than do ileal atresias. When the cases in our series which demonstrated both extrinsic and intrinsic lesions of the duodenum are grouped with the duodenal lesions, the apparent difference between the two groups disappears, and they join the overall group of complete obstructions which produce a mortality of 75 per cent.

When our cases are grouped by years (Table III), it seems justifiable to conclude that the mortality has improved to some extent as a result of better and earlier diagnosis, more blood, and the use of antibiotics. In any con-

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clusions drawn from such figures, however, it must be considered that the relative incidence of cases of complete obstruction in any one group will considerably affect the mortality rate.

TABLE III.—*Comparative Mortality*

	Cases	Mortality
1924-1938.....	11	81%
1939-1948.....	33	51%*
1944-1948 (U. H.).....	20	35%†

* During this interval supportive therapy was significantly improved.

† In this group earlier diagnosis was a probable factor. The fact that this group included 33 per cent intrinsic lesions as compared with 64 per cent intrinsic lesions for the entire series may have influenced the mortality also.

Table V shows some of the possible causes of mortality which the surgeon can improve. Even if it were theoretically possible to eliminate all these, however, the surgeon would still be handicapped by the incidence of prematurity and associated cardiac defects.

TABLE IV.—*Factors in Mortality*

Of infants known to be premature mortality was.....	60%
Of infants with associated anomalies, chiefly cardiac, mortality was.....	92%
Those with complete obstruction, mortality.....	75%
Those with incomplete obstruction, mortality.....	50%

There was no direct correlation between the age of the infant at the time of operation except in the case of intrinsic lesions where delay in operation seemed to influence the mortality.

SUMMARY

The chance of survival of the newborn infant with intestinal obstruction has increased during the past quarter century due to improved diagnostic, supportive and operative technic, but not to the extent achieved in adults.

TABLE V.—*Factors in Mortality of Particular Concern to the Surgeon*

Tabulation of Possible Surgical Errors in Authors' Series	
Incomplete operation.....	11
Inadequate blood.....	4
Technical errors	
Poor choice of anastomosis.....	1
Stomach not decompressed.....	2
No complementary ileostomy.....	6
Ileostomy only.....	3
Total.....	12
Total.....	27
Less causes duplicated.....	4
Net total.....	23
Total deaths in series.....	25

We have presented a group of cases from three large urban hospitals, operated upon by a number of surgeons, and have reviewed some of the errors in management that may have contributed to the high mortality rate.

Diagnostic methods have been summarized. The history and physical findings are usually characteristic and are verified by roentgenograms.

The administration of blood and electrolyte solution before, during, and after the operation is of prime importance.

Factors contributing to high mortality rate are: the high incidence of prematurity and cardiac anomalies, delay in diagnosis and hence operation, inadequate supportive therapy, and inadequate or unphysiologic operative management.

The most significant single factor seems to be the presence or absence of complete obstruction.

Surgical errors rank high as probable causes of failure.

Penicillin given before, during, and after operation reduces the incidence of peritonitis.

Anesthesia, surgical approaches, and specific operative procedures are probably less important in determining results than are a thorough understanding of the anatomical and physiological problems peculiar to the lesions. Completeness in exploration, and the use of primary, definitive surgery together seem to offer the best chance for survival of the infant. Partial procedures are to be avoided at all cost. The use of postoperative decompression is of major importance.

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DISCUSSION.—DR. THOMAS H. LANMAN, Boston: I think this presentation by Dr. Glover shows what can be done with careful technic and careful attention to the many minute details so necessary to success in dealing with these young patients. His results are remarkably good and though ours at the Children's are perhaps a little better, I think it will be only a short while before ours may be surpassed by those of Dr. Glover.

The important thing, when dealing with these malrotations, is a clear understanding of the embryology. Not until this fundamental knowledge was appreciated did we get any lowering of the mortality in midgut volvulus, associated with malrotation. In the other conditions, Dr. Glover's figures correspond with ours, in that the higher the atresia or stenosis, the better are the results. We have had a 61 per cent recovery in the cases of obstruction in the duodenum. Decompression proximal to the lesion, I think, is of great importance, but in our experience the nasal catheter to the stomach seems to be better tolerated than Dr. Glover has mentioned. We do not sew a catheter in the bowel or stomach routinely as he has described, and believe that in most cases it is not necessary or desirable.

In the cases of malrotation, as you have seen from the motion picture, it is vital to obtain a very wide exposure and so be able to see very clearly just what the condition may be. It is futile to attempt to see or to treat what is wrong, through an inadequate incision.

An understanding of the embryology has resulted in very much better treatment, but we must go further in our studies of the underlying cause of these conditions. In looking over our cases to bring them up to date last year, we came across a rather disturbing fact. It suggests the importance of the basic underlying cause of all these malformations. As Dr. Glover pointed out, these anomalies often are multiple. In considering associated anomalies, the disturbing fact is this:

In our last 17 recoveries in the surgical treatment of duodenal atresia, four patients

now are proved Mongols and two others are mentally deficient. These cases are now three to five years after operation. Obviously one cannot, with any security, make a diagnosis of Mongolian idiocy on the first day of life, though in two of these cases, we did record this possibility.

We must go on improving our surgical technic, our knowledge of fluid balance, and all those details which are of such great importance to surgical success. We must not discourage attempts to cure these malformations, but I do think that the coming generation should be stimulated to find out *why* they occur, and to me this is now the greater challenge.

We have a high per cent of mentally deficient patients in this recent series of successfully operated cases. Perhaps one could argue that these children were born 20 years too late, because 20 years ago they would, presumably, all have died. I do not agree with such a premise, but rather I believe we should go further in the study of these conditions than in the mere improvement of surgical technic.

I would prefer to accept this challenge of the need for further study than to take a rather simpler explanation that was offered to me last evening by a colleague, who remarked that these figures on mental deficiency merely confirmed his impression that Boston was no longer an intellectual center.

DR. EDWIN M. MILLER, Chicago: Mr. Chairman and Gentlemen, I hesitate to discuss this interesting paper of Dr. Glover for fear of not being able to add anything of real importance. Great strides, indeed, have been made in this field since the first successful operation for atresia of the small bowel by Fockens of Rotterdam in 1911, and several members of the American Surgical Association have made worthwhile contributions, particularly Dr. Ladd, Dr. Gross, and Dr. Lanman of Boston and Dr. Donovan of New York, Dr. Wangenstein of Minneapolis, and Dr. Willis Potts of Chicago.

As I see it, the all-important thing is early diagnosis, and in order to obtain an early diagnosis the chief problem is to bring the matter effectively to the attention of those who first see these little infants with congenital obstruction, namely, the obstetrician, the pediatrician, and the men in general practice.

I would like to point out one or two things which are important:

1. The use of barium by mouth is not advisable in making a diagnosis and is not necessary, as a plain x-ray film of an atresia of the duodenum will clearly show the stomach and duodenum distended with air, and if the obstruction is in the small bowel, the dilated loops will be easily seen. The value of barium, if used at all, is when employed by enema, as then it will help to rule out an obstruction in the rectum or at the anus, and when it flows freely into the large bowel will reveal the pressure or absence of an incomplete rotation of the colon, thus giving information very important to the surgeon.

2. It is imperative before operation to deflate the obstructed bowel with a Levine tube or a small-sized (No. 12) Miller Abbott tube if possible, in order that the abdomen can be widely opened and the obstruction adequately dealt with so that the use of an ileostomy may be avoided.

These points are here emphasized by four lantern slides which show (1) the ease of diagnosis of an atresia of the ileum by the plain x-ray film, (2) the successful anastomosis after adequate deflation of the bowel, (3) the good progress of the infant about six weeks later, and (4) the G. I. follow-through with barium by mouth three months after surgery.

The moving pictures shown by Dr. Glover in dealing with a high obstruction due to volvulus and malrotation have been very instructive.

DR. WILLIS J. POTTS, Chicago: The history of one of three similar patients seen recently is interesting in connection with this subject of intestinal atresia so well presented by Drs. Glover and Barry.

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This three-day-old child had all the signs and symptoms of congenital atresia of the bowel. The x-ray picture (slide) shows typical dilated intestinal loops containing fluid levels. The infant had had no bowel movement. During the operation under ether anesthesia the infant passed a huge meconium stool. No obstruction was found and the abdomen was closed. Attention was promptly called to an article which appeared in the American Journal of Diseases of Children in January, 1948, by Zuelzer and Wilson of Detroit, "Functional Intestinal Obstruction on a Congenital Neurogenic Basis in Infancy." Their description of cases showing all the signs of congenital atresia of the bowel but actually having no mechanical obstruction made the diagnosis for us. Typically the infant again developed signs and symptoms of complete intestinal obstruction requiring a transverse colostomy.

Since the area of agensis of the myenteric plexus is usually confined to the descending colon it has been advised that the descending portion of the colon be resected later and that the transverse colon be anastomosed to a suitable stump of the rectum.

DR. DONALD M. GLOVER, Cleveland: We are much indebted to Dr. Lanman, Dr. Miller and Dr. Potts for their discussion.

In regard to Dr. Lanman's comment that at the Children's Hospital they have had little difficulty with the presence of a tube in the baby's pharynx, I must admit that we have also had some patients who seemed to tolerate it fairly well. Some of them, however, develop edema of the pharynx from the presence of the tube, and in some instances there was tracheal aspiration of regurgitated gastric contents which we believed was at least partly due to the presence of the tube. We do not at present have bilumen tubes small enough to be satisfactory for use in small infants, and it seems safer to have feeding and aspiration tubes inserted through the gastric wall than to depend upon a tube introduced through the pharynx which can serve only as a feeding tube or an aspiration tube, but not both.

Dr. Lanman has called attention to the associated defects. We hope that the present efforts of the obstetricians and internists to prevent prematurity and maternal infections during pregnancy may reduce the incidence of these defects.

Referring to Dr. Miller's comment about ileostomy, there have been at least two cases reported where survival has followed the primary use of ileostomy alone. Dr. Miller also raised the question about the possibility of future obstruction in cases of malrotation and volvulus in which the colon and duodenum have been freed from their lateral peritoneal attachments. Among the last ten cases operated upon in this manner, we have had one case of recurrent obstruction which was not, however, due to denudation of peritoneum. A number of cases will be found in the literature which demonstrate the possibility of a recurrent obstruction where the colon and duodenum have not been completely mobilized, as advised by Ladd. From the patients we have had an opportunity to follow, we have encountered no difficulty from deperitonealization. We have been impressed with the fact that the peritoneum of the newborn infant covers defects rapidly.

The question as to whether or not the colon should remain on the left side, in the fetal position, has been argued. Dr. Ladd feels that it should and most of us, I believe, feel that it is safer in that position. We have on occasion, however, deliberately placed the colon on the right side of the abdomen without fixing it in any way and subsequent roentgenograms, taken years later, have shown that the cecum remained in its normal position on the right side although the duodenojejunal junction retains its vertical position.

The interesting case presented by Dr. Potts brings up several important points which, due to time limitations, we shall not attempt to discuss.

GASTRO-INTESTINAL GAS

OBSERVATIONS ON BELCHING DURING ANESTHESIA, OPERATIONS AND
PYELOGRAPHY; AND RAPID PASSAGE OF GAS*

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STUDIES ON THE ORIGIN of gastro-intestinal gas support the theory that swallowed air is its chief source. The literature on the subject is voluminous and only a few pertinent articles will be referred to.

Kantor¹ in 1918 presented the older historical background on the subject and Alvarez's² comments are thorough and interesting. McIver, Benedict and Cline³ in 1926 showed that cats with peritonitis had considerable gaseous distention of the stomach and intestine, but if the pylorus was ligated at the time of the peritoneal contamination, then the stomach was dilated without distention of the intestines. The importance of swallowed air was obvious, and, using gastric suction in patients, these authors were able to reduce materially the incidence of postoperative distention. Wangenstein⁴ in 1932 instituted the very important use of continuous gastro-duodenal suction-siphonage in decompressing certain types of acute mechanical intestinal obstruction, and with Paine and Carlson⁵ in 1933 showed that the same procedure would often remove from 2000 to 3500 cc. of gas daily from postoperative surgical patients, and thus markedly reduce the incidence of postoperative distention. Wangenstein and Rea⁶ in 1930 presented their classical experiment further indicting external air as the main source of gastro-intestinal distention by showing that the gas content of obstructed ileal loops in dogs was greatly reduced if at the time of producing the obstruction the cervical esophagus was also divided and the distal end closed. In earlier experiments it had been learned that if the distal end was left open the animal swallowed as much air as a dog with the esophagus intact. Singleton, Rogers and Houston⁷ in 1942 stated that postoperative distention in patients undergoing abdominal operations did not occur as long as continuous suction was applied through an inlying gastric tube. They emphasized the prevention of gaseous distention by the preoperative institution of the procedure rather than its use to relieve distention later. The present widespread use of this valuable advance in abdominal surgery is due to the work of these various investigators.

The authors' interest in this subject centers mainly on how atmospheric air enters the esophagus and stomach. Actual swallowing of air does play a part in many cases, but there must also be other mechanisms involved, particularly to account for the occasional large and rapid accumulations of gas.

* Read before the American Surgical Association, St. Louis, Mo., April 21, 1949.

Morris, Ivy and Maddock⁸ noted the paucity of observations on actual swallowing of air by distended patients and reviewed pertinent comments on acute gastric dilatation, air-sucking and esophageal speech, conditions under which air is known to enter the esophagus and stomach without swallowing. In order to study possible mechanisms involved they attempted by a large number of animal experiments to produce acute gastric distention, but were unable to do so with any degree of constancy. Using human subjects, however, they were able to show that:

1. Attempting actively to breathe against a closed glottis can produce negative pressures in the esophagus and stomach up to 30 cm. of water.

2. The superior esophageal constrictor is a very important sphincter normally closed, but opening on deglutition to allow food and drink to pass into the esophagus. This sphincter can be relaxed consciously by some individuals and unconsciously by others. The muscular tube of the esophagus is interesting in that at least the upper part is striated.² The superior esophageal sphincter was first described by Killian⁹ in 1908 and is found at the pharyngeo-esophageal junction where a fold of mucosa and the transverse fibers of the inferior pharyngeal constrictor muscle form the sphincter.

The combination of the negative pressures stated in (1) above and intubations or relaxations of the superior esophageal sphincter permitted the following observations. In reading them over it is evident that the processes described are all of the same nature, with only minor variations, depending upon ways of opening the sphincter and how the negative intra-esophageal pressure was produced.

3. With the superior esophageal sphincter intubated with a Levine tube to the stomach, the negative pressure of each attempt to breathe against a closed glottis easily drew from 50 to 160 cc. of air from a spirometer into the stomach. With a few such efforts gastric gas quickly amounted to 400 to 500 cc.

4. With the superior esophageal sphincter relaxed, as can be done by many individuals, the negative pressure of attempting to breathe against a closed glottis easily drew 1000 to 2000 cc. of air into the esophagus in a period of three to five minutes. "Air-suckers" to us are individuals who know they can do this, and control the act. "Aerophagics" carry out the same procedure, but are the highly nervous or hysterical individuals who do not know or will not recognize what they are doing to ingest air. The relationship between nervousness and gastro-intestinal gas has been stressed by many authors and will be emphasized later in this paper.

5. With the superior esophageal sphincter partially relaxed, as in sleep, attempting to breathe against an obstructed airway—tongue dropped back and snoring—resulted in the aspiration of air into the stomach.

6. Along with learning how to relax the superior esophageal sphincter the laryngectomized patient can place a finger over the tracheotomy opening and on trying to breathe produces an increased negative intra-esophageal pressure which draws air into the esophagus, and stomach to some extent. With con-

trolled eructations of the air "esophageal speech" is possible. The intake procedure is fundamentally the same as air-sucking.

7. When the superior esophageal sphincter is intubated with a Levine tube to the lower esophagus the negative pressure of respirations can easily draw air in from a spirometer. For five subjects the following average amounts were so aspirated per minute: normal quiet respirations—39.5 cc.; moderately deep respirations—43.7 cc.; deep respirations—91.9 cc.

The esophageal speech patient with practice no longer needs to place his finger over the tracheotomy opening to take air into the esophagus, but learns to "aspirate" or "inspire" the air with respiratory movements, as done by the above subjects.

From these observations the importance of the superior esophageal sphincter, and the effect of respiratory movements in the mechanism of air entry into the upper gastro-intestinal tract, are apparent. It is believed that

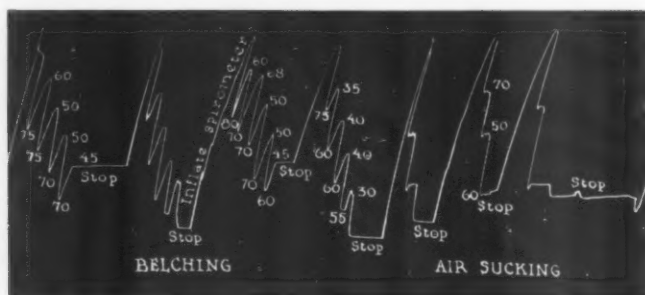


FIG. 1.—Air exchange with belching and air sucking. With belching some air is retained, the aspiration figures in cubic centimeters on the left side being greater than the eructation figures on the right side. When asked to suppress the eructations and perform air-sucking for three efforts a total of 180 cc. were aspirated. A. B. was then unable to hold the air and felt some discomfort. A voluminous belch followed.

many conditions, intra-abdominal and elsewhere, may originate reflexes changing the tone of the sphincter and varying respiratory movements with resulting aspiration of air into the esophagus and stomach. The great diversity of diseases in which acute gastric dilatation has occurred⁸ support the opinion that a reflex phenomenon is involved. In many instances it may be discomfort, nervousness, and apprehension associated with the disease or injury and its treatment, that starts the unconscious aspiration of air.

To learn more about gas in the gastro-intestinal tract this paper presents studies on: (1) belching, (2) swallowing movements, and the entrance of air into the stomach during anesthesia and operations, (3) the rate of passage of air through the gastro-intestinal tract and (4) meteorism during pyelography.

BELCHING

Alvarez² lists six different kinds of belches and points out that many of the individuals afflicted with more than the usual polite belch after a meal

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are nervous, worried, irritable, distracted and hyperactive people. He has frequently seen the chronic belcher under the fluoroscope and notes that most of the air stays in the esophagus and does not descend into the stomach.

Frequent belching is a modification of air-sucking or aerophagy. The individual who can repeatedly belch on request knows how to relax the superior esophageal sphincter, does so, and then tries to breathe in with the glottis closed.¹⁰ The air thus entering the esophagus is immediately belched back. The subconscious or unintentional frequent belcher is invariably a nervous individual who does about the same thing, probably taking in the air by a less apparent respiratory effort.

It is known that frequent belching often produces a sense of fulness in the epigastrium and probably is the source of considerable amounts of air entering the stomach. Belching was therefore studied to obtain some quantitative data.

TABLE I.—*Summary of Air Exchange with Belching*

Subject	No. of Belches	Cc. of Air					
		Aspirated		Eructated		Retained	
		Total	Av.	Total	Av.	Total	Av.
1.	9	815	91	760	84	145	16
2.	8	235	29	200	25	35	4
3.	8	710	89	405	51	305	38
4.	13	580	45	470	36	110	8
5.	18	740	41	335	19	405	23

(Frequent belching can result in the retention of considerable air. With a patient lying down this can easily pass into the intestines and produce distention.)

Method. Normal young males who could belch at will were used in this experiment. They performed the act with the nose closed by a soft clamp and the mouth closed around a glass tube connected to a recording spirometer and kymograph.

Result. It was easily demonstrated, as has been described before, that these voluntary belchers take in air by air-sucking and then immediately eruct the air. Two distinct sounds can be heard with this process,¹ the first with the air entering and the second as it is belched back. "Cribbing" in horses is the same process,^{10, 10a} and Wyllie similarly described the two sounds.

A typical kymograph tracing (Fig. 1) shows that with belching the amount of air aspirated into the esophagus was greater than the amount of air eructated and some air probably passed into the stomach.

A summary for the five subjects of this experiment is shown in Table I. The totals and average amounts of air aspirated, eructated and retained are quite impressive and, with the subject lying down, this air could easily pass into the intestines and produce distention.

Belching often comes on as a manifestation of nervousness, and Fig. 2 shows marked gastro-intestinal distention in a nervous and apprehensive surgical patient who was repeatedly belching. It is recalled that in previous

years it was not uncommon to ask a patient with distention if he were passing gas rectally and to have him answer, "No, but I am belching up gas." With the data of this study it is realized that the belching may have been the process responsible for the distention.

AIR INGESTION DURING ANESTHESIA AND OPERATIONS

In their study of postoperative distention McIver, Benedict and Cline³ considered the rather frequent finding of gas in the stomach and stated that "It is well known that a great deal of air may be swallowed during the early stages of anesthetization." They observed 115, 67 and 54 swallowing move-



FIG. 2.—Marked gastro-intestinal distention in a surgical patient from repeated belching. There was considerable passage of flatus during the time of the distention. When J. S. stopped belching by request the distention rapidly subsided.

ments in three patients undergoing etherization, but no measure was made of the amount of gas taken into the stomach with these swallows. On the other hand Davis and Hansen¹¹ determined the amount of air taken into the stomach during operations and concluded that much of it entered during the induction of anesthesia, but no record was made of swallowing or other possible modes of gas entrance.

GASTRO-INTESTINAL GAS

It was our impression that frequent swallowing did not take place during the course of an anesthetic and operation, yet occasionally the stomach distended with air during that time. To learn more about swallowing and to repeat Davis and Hansen's work, a series of 23 patients was studied.

Method. A Levine tube was inserted into the cardiac end of the stomach from 60 to 90 minutes prior to the induction of anesthesia. Continuous suc-

TABLE II.—*Air Ingestion During Anesthesia and Operations*

Number, Sex and Age			Operative Procedure	Induction Period			Operative Period		
				Time Min.	Swal- lows	Gas Cc.	Time Min.	Swal- lows	Gas Cc.
Group A. Spinal and Pentothal Anesthesia									
1.	F	57	Lysis abd. adhes.	20	0	0	74	4	100
2.	F	49	Abd. perin. res.	20	0	0	178	0	75
3.	F	73	Abd. perin. res.	20	0	0	136	0	120
4.	F	55	Abd. perin. res.	10	0	0	210	0	100
5.	M	61	Amput. thigh.	15	0	0	55	0	30
6.	F	38	Cholecystect. liver biopsy	10	0	0	78	0	50
7.	M	74	Abd. perin. res.	22	0	0	206	0	780
Group B. Inhalation Anesthesia NO ₂ or C ₂ H ₄ or C ₂ H ₆ + O ₂ + ether									
8.	M	63	Cholecystectomy	8	0	0	116	0	130
9.	F	62	Cholecystectomy and appendectomy	8	2	0	90	0	70
10.	M	39	Cholecystectomy and resection duod. divert.	5	3	30	135	0	0
11.	F	52	Cholecystectomy, choledochostomy	5	3	50	86	0	25
12.	F	71	Transverse colos.	4	0	0	55	0	0
13.	F	54	Choledochostomy	10	2	50	88	0	50
Group C. Cyclopropane and Curare									
14.	F	57	Cholecystectomy, choledochostomy	6	0	0	120	0	130
15.	M	56	Cholecystectomy	4	3	0	116	0	0
16.	M	62	Cholecystectomy	5	0	0	86	0	0
17.	M	49	Splenectomy	7	0	0	98	0	0
18.	F	47	Cholecystectomy, appendectomy	6	0	0	98	0	25
Group D. Cyclopropane and Curare									
19.	M	39	Gastroenterostomy, Vagotomy	9	3	75	170	0	385
20.	F	70	Cholecystectomy	4	2	50	60	0	825
21.	F	57	Cholecystectomy, excl. lipoma stomach	4	1	10	113	0	1600
22.	F	53	Ventral hernia	6	0	20	177	0	1700
23.	M	30	Partial gastric resection	6	5	50	204	0	250
Average					1.0	14.5			
For inhalation anesthesia					1.5				

Important Findings: 1. Swallowing movements were infrequent. 2. Air intake high with obstructed respirations—case 7. 3. Air intake high with curare plus positive pressure anesthesia.

tion was applied immediately to empty the stomach and was continued throughout the remainder of the preoperative and operative period. By measuring the amount of water displaced in the upper bottle of the Wangensteen suction apparatus, the amount of gas returned from the stomach was determined. The anesthetist* counted the swallowing movements during

* This work was done with the assistance of Dr. Mary Karp, Chairman of the Dept. of Anesthesia, Wesley Memorial Hospital, and will be reported later in detail with her.

the induction of anesthesia by placing a finger over the patient's larynx. One of us (J.B.) recorded the amounts of gas returned, and the coincident actions of the patient, the surgeon and the anesthetist for the remainder of the procedure.

Results. Of the 23 patients studied, all operations except one, No. 5, were laparotomies. The usual preoperative medication consisted of morphine sulfate 10 mgm. and atrophine sulfate 0.4 mgm.

From the summarized data shown in Table II it is evident that during the swift induction of a modern inhalation anesthetic there are very few swallowing movements, our average of 1.5 per patient being far less than the 79 average observed by McIver, Benedict and Cline³ during the longer induction of an ether anesthetic. We believe these swallowing movements are largely manifestations of nervousness and they did not result in appreciable amounts of gas entering the stomach.

During the operations only small amounts of gas entered the stomach of the majority of patients. Excluding the exceptions, patient No. 7 and all those of Group D which will be discussed further, our figures of 0 to 130 cc., average 53 cc., are less than, but not significantly different from, Davis and Hansen's¹¹ average of 143 cc.

Patient No. 7 of Group A had a 780 cc. intake of air during the operation, which we believe was due to his attempts to breathe against a closed glottis. The observer noted that the jaw dropped occasionally during the operation and there was a snoring and partially obstructed respiration. Air could thus not easily pass into the trachea, and the negative intra-esophageal pressure aspirated air downward to the stomach. We have seen distention develop in other patients with an obstructed airway. This factor, along with the more important one of decreased oxygenation and cyanosis, give great reason why the respiratory passages must be kept open.

It was noted by the observer that the ordinary manipulations of the viscera attendant upon an abdominal operation did not result in gas entering the stomach.

The patients of Group D were of special interest. Their anesthetic was cyclopropane and curare, the same as Group C, but 250 to 1700 cc. of gas were aspirated from their stomachs. The D group had some intercostal paralysis following the injection of curare and slight positive pressure was used to augment respirations. It was thought that the curare considerably relaxed the superior esophageal sphincter and this, plus the pressure anesthesia, forced some gas into the stomach.

Anesthetists have long known that gastric dilatation is a common complication of positive pressure anesthesia and recently¹² a warning was given to be ready to aspirate air from the stomach when curare is used.

The results of this experiment fit well with clinical experience. At most laparotomies there is no troublesome distention of the stomach, but occasionally it is observed by all surgeons, and it occurs without swallowing. Luckett,¹³ in reporting a case in which acute distention occurred during surgical treat-

ment, stated, "I could distinctly feel and hear large gulps of air entering the stomach, and hear a noise in the throat, yet the patient was not swallowing, that is, the thyroid cartilage was apparently still and there was no visible motion in the throat."

A remarkable case report was recently received¹⁴ in which the patient "inspired" air into the esophagus with resulting distention and spontaneous perforation of the stomach. Roentgenograms of the consequent enormous pneumoperitoneum, and a brief description of the case, are given in Fig. 3. There can be no doubt that relaxation of the superior esophageal sphincter and respiratory aspiration of air blew this patient up.

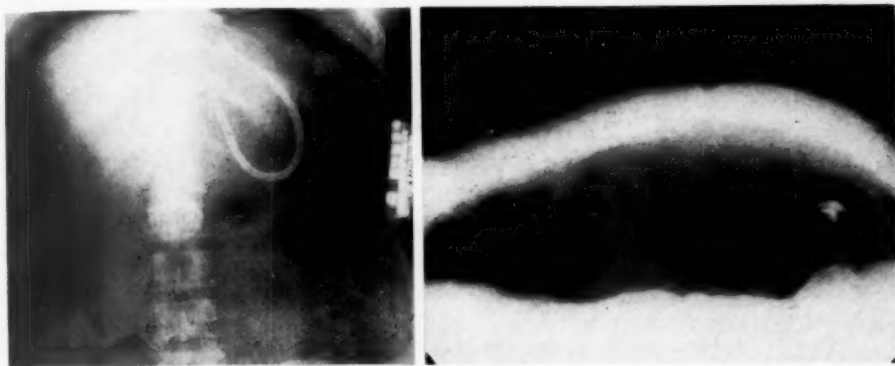


FIG. 3.—Enormous pneumoperitoneum following spontaneous rupture of a stomach distended by inspired air during a minor operation under sodium pentothal anesthesia. Mrs. G. H., a woman, age 47 years, was admitted to the hospital on June 16, 1947, for removal of a root fragment of the right first lower premolar tooth. A chronic draining sinus at that point necessitated the surgery. History and physical examination and laboratory data were otherwise normal. B.P. 134/78. Pre-operative medication was morphine sulfate gr. 1/6 and atropine sulfate gr. 1/150. The patient arrived in the operating room in good condition. B.P. 124/80. An intravenous sodium pentothal anesthesia using a 2.5 per cent solution was started at 8:10 A.M. and a total of 0.75 Gm. were given. Anesthesia to first plane appeared within 45 seconds. At 8:13 a Guedel pharyngeal airway was inserted and a sibilant, hissing sound audible to all those in the operating room was emitted by the patient. The sound resembled the hiss of an angered goose rather than the high pitched, strained crowing of laryngo-spasm. It persisted continuously, with only minor variations in intensity and was completely inspiratory. The anesthetist felt quite certain that the airway could not have slipped into the esophagus. The anesthesia was otherwise uneventful; B.P. and pulse were normal. At 8:15 oxygen at 2 liters per minute was started through a small nasal catheter. "Moderate" abdominal distention was noted while draping the patient. At 8:15 the operation was started and was finished at 8:27. "Enormous" abdominal distention was noted when removing the drapes. The abdomen was tympanitic and no intestinal sounds could be heard.

On return to the patient's room a Wangensteen tube was inserted, but no gas or fluid was obtained. B.P. was now 90/60. At 10:00 A.M. a second passage of the Wangensteen tube brought up a small amount of blood. Scout roentgenograms of the abdomen revealed the massive pneumoperitoneum. The diagnosis of a perforation of the stomach was made and the patient was returned to surgery for a laparotomy. When the abdomen was opened, air escaped under pressure with the sound of a tire being rapidly deflated. The peritoneal cavity was free of fluid, blood or food particles. The lower half of the stomach and duodenum were normal to inspection. The upper portion of the stomach was exposed and a 4.5 cm. longitudinal rent was found about 1 cm. anterior to the lesser curvature, the proximal end of the tear being 2.5 cm. below the cardio-esophageal junction. This clean edged tear was through normal stomach tissue. It was closed and the patient made an uneventful convalescence.

THE RAPID PASSAGE OF AIR THROUGH THE GASTRO-INTESTINAL TRACT

Gastro-intestinal gas that appeared quickly was disturbing to us at one time because the source as "swallowed air" was not readily apparent. But with a better understanding of air sucking, aerophagy, belching, the action of the superior esophageal sphincter, and negative esophageal pressures from inspiratory efforts, the possible mechanisms of the rapid flow of air down the esophagus became evident. Fortunately, the rapid accumulations of gastric gas, rather than the slow increments, offered the best chance of observing how and under what conditions it entered the esophagus. In this regard many comments have been made on the marked increase in intestinal gas frequently seen in the short time from the first to the last roentgenogram of patients undergoing pyelography. Many observers—radiologists, urologists, etc.—accept the general impression that "swallowed air" is the source of this gas the same as in other flatuositities. Oppenheimer¹⁵ and Begg,¹⁶ however, offer different theories.

Oppenheimer¹⁵ in 1940 noted that excessively large amounts of gastro-intestinal gas appeared during retrograde pyelography when this procedure produced pain, and this led him to study the relationship between pain and gaseous distention. He found that in 82 instances of severe pain, such as with fractures of the extremities and spine, gonococcal arthritis, sciatica, lumbago, toothache, trigeminal neuralgia, herpes zoster and dislocations no gaseous distention was observed. On the contrary, in numerous cases of renal colic, biliary colic, duodenal ulcer, acute appendicitis and salpingitis the type of gaseous distention was identical with that found during retrograde pyelography. In 14 of his patients with urinary disease intravenous pyelography was done with complete absence of pain, yet gaseous distention developed. Accordingly, Oppenheimer believed that pain in itself was not responsible for the appearance of gas in the bowel, but that some abdominal diseases may cause both pain and gaseous distention.

Oppenheimer observed roentgenographically in man that ureteral catheterization and distention of the renal pelvis with fluid or oxygen was followed by rapid overfilling of the stomach, small intestines and colon with gas, and stated that the large amounts seen within a few minutes could not possibly be due to abnormal fermentation or diffusion from the blood stream. To account for the source he offered the thesis that the small amount of gas always present in the intestines quickly expanded to fill the intestines when they became atonic due to inhibitory reflexes which arise from renal or biliary colic, pyelography, etc.

This thesis is untenable because a given amount of gas cannot expand into a larger space without a reduction in pressure, and the soft intestinal tube and flexible abdominal wall will not be supported in reduced pressure. Except for moments of active peristalsis intestinal gas pressure is close to atmospheric pressure.

Begg¹⁶ in 1948, in writing on a rational theory of intestinal distention and its urological application, contended that gas pains and distention may be

completely obviated provided nothing whatever is given by mouth or rectum during the inevitable postoperative non-peristaltic period. He did not believe that distention was due to air swallowed during and after the operation for the following reasons: (1) The theory is inapplicable to distention accompanying spinal lesions, lightning stroke, renal colic, anuria, etc., unless one is to suppose that the victims become suddenly addicts to aerophagy. (2) It is incompatible with the observed fact that postoperative patients do not distend if given no fluid, no matter what air they may have swallowed. He further stated that if it were contended that the air was swallowed with the fluid, it would be hard to imagine that a single drink would initiate progressive and increasing distention as he has observed.

Thus, finding the swallowed air theory to be unsatisfactory, and the role of food fermentation disproved, Begg considered the only remaining possibility to be gas derived from the blood, and nitrogen the important gas, it being available to the bowel by "intestinal respiration" and absorbed if it is in excess. The passage of nitrogen to the bowel and back to the blood depends on the physical laws of diffusion of gas, and Begg considered that any factor which, when the dynamic function is in abeyance, reduces the tonus, increases the potential capacity of the bowel lumen and permits the inflow of gas. He stated further that fluids and food reaching the stomach during the postoperative refractory period cause this organ to contract on its contents, leading to a reflex reduction in tone of the intestines which enables the blood gases to flow in to fill the increased space in the lumen. He cited the marked increase in intestinal gas when an ureteral catheter is passed, and the quick influx of gas into the bowel following the injection of Uroselectan, as further evidence of the theory of rapid diffusion of nitrogen into the bowel, given the requisite conditions.

The authors believe that giving nothing by mouth to postoperative patients reduces the possibility of gaseous distention, but certainly does not eliminate it entirely, and relative to Begg's opinion that swallowed air cannot be the main source of gastro-intestinal gas unless "the victims become suddenly addicts to aerophagy" the evidence of this study shows that this is exactly what may take place, if one uses the term aerophagy in a broad sense covering the esophageal ingestion of air without swallowing.

The time element for the accumulation of large amounts of air in the stomach is known to be rapid in acute gastric dilatation,⁸ air-sucking and aerophagy. The time element for the almost immediate passage of gastric gas into the small intestine and its arrival at the cecum and anus within a few minutes is not well known. Usually gas is not thought of as passing along any faster than food. Actually it does, and this point was first studied by Magnusson.¹⁷

In 1931 Magnusson was interested in meteorism in pyelography. He dismissed gas formation from intestinal decomposition and diffusion from the blood as possible sources and believed that the main bulk of the gas consisted of air that had passed down the esophagus, probably by some

process of aerophagy or air-swallowing. Magnusson's important point was that to account for the rapid colonic meteorism in pyelography the "swallowed air" must pass out of the stomach and through the small intestine in a very short space of time. To confirm this impression he filled the colon of normal adult subjects with an opaque enema so that air coming into the cecum could be easily seen. He then turned the subjects on their left side to place the pylorus upward and injected air into their stomachs. The progress of the air was determined by frequent roentgenograms and the results are shown and compared with the passage of food in Fig. 4.

It was considered that a further investigation of this rapid air passage should be carried out.

Method. For these experiments young, male, medical students were used. No purgatives or enemas were given and a normal breakfast was eaten about three hours before the experiment. An initial scout film of the abdomen showed the existing amount of gastro-intestinal gas, and usually the stomach was found empty. A 16 F. Levine tube was then introduced

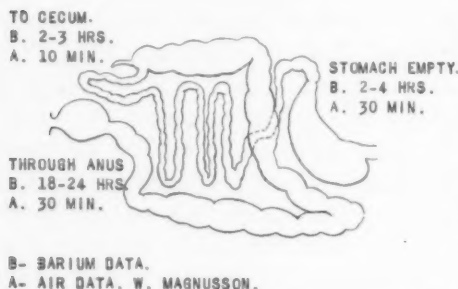


FIG. 4.—Diagram showing the rapid passage of air compared to barium through the adult gastro-intestinal tract. (W. Magnusson¹⁷.)

through the nostril into the middle esophagus, a distance of about 30 cm., and was connected to a graduated spirometer by a tube having a one-way valve allowing gas to pass only in the direction of the esophagus. The subjects then lay on the radiographic table on their back or side just as they wished. In most subjects a 30 F. mushroom catheter was inserted into the rectum and flatus collected by means of a water displacement apparatus. The spirometer was then filled with air, 100

per cent oxygen for one experiment, and on moderately deep respirations the negative pressure produced in the esophagus drew air from the spirometer into the esophagus, from which it passed into the stomach.

Besides the initial roentgenograms,* others were taken when 500 cc. and 1000 cc. of air had been aspirated and at later intervals to show the extent of the flatulence. Careful records were made of the symptoms of the subjects, cramping abdominal pains if any, the degree of abdominal distention as measured at the umbilicus, the time of first passage of flatus, and the total amount passed.

Results. The majority of subjects were allowed to aspirate 1000 cc. of air which they did in about 30 minutes. W. H. took in 1650 and 2000 cc. in approximately the same time.

It is suspected that more air may have entered the stomach of some sub-

* This part of the study was done with the assistance of Dr. Earl Barth, Assoc. Prof. of Radiology, Northwestern University, and will be reported later in detail with him.

GASTRO-INTESTINAL GAS

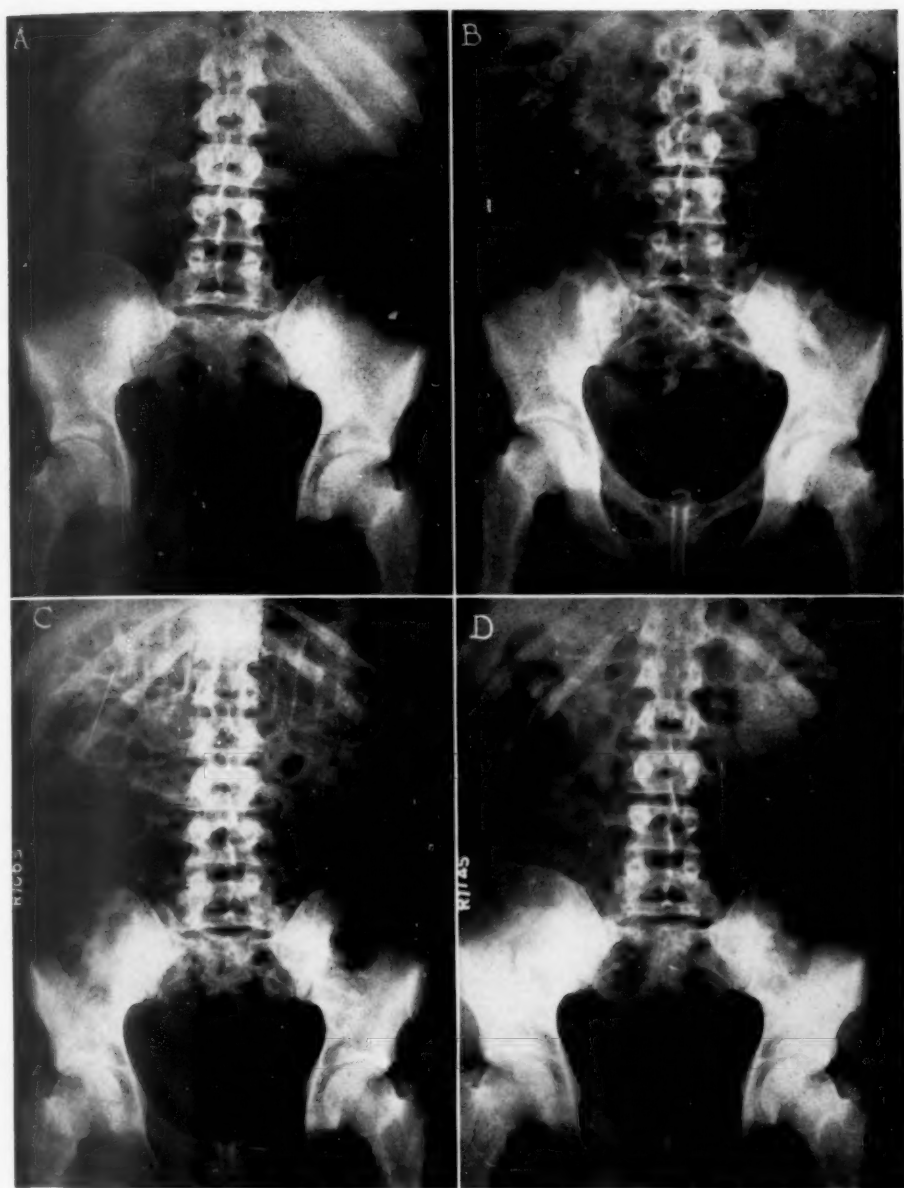


FIG. 5.—Roentgenograms showing rapid passage of 1000 cc. of oxygen. (L. S.²) (A.) Before the passage of the Levine tube. No gas in the stomach or small intestine and only a small amount in the ascending and descending colon. Oxygen aspiration, which seemed to be no different than air aspiration, was then started. At 18 min. increased gas was seen in the cecum by a following roentgenogram. (B.) At 28 min. Shows the distribution and distention produced by 1000 cc. of gas. Esophageal tube had just been removed. Abdominal girth at umbilicus increased only 2 cm. At 36 min. the first flatus was passed. (C.) At 53 min. Considerable gaseous distention although 500 cc. of flatus had been passed. (D.) At 110 min. Less general distention but still some gas in the distal three-fourths of the colon. Flatus passed 800 cc.

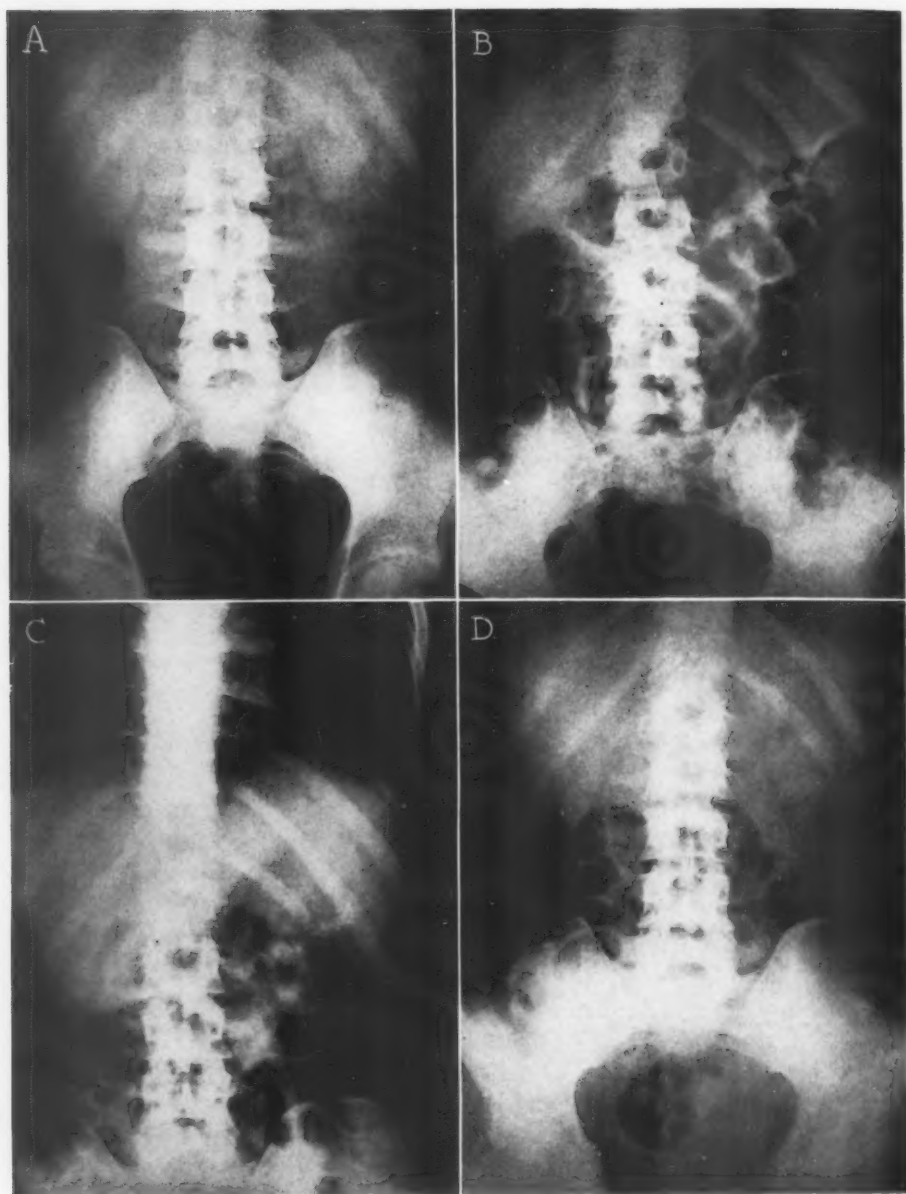


FIG. 6.—Roentgenograms showing rapid passage of 2000 cc. of air. (W. H.) (A.) Initial film showing only a small amount of gas in the cecum, descending colon and rectum. (B.) At 17 min., 1000 cc. of air had been aspirated. The stomach and intestines are considerably dilated. The first flatus had just been passed. A previous film at 8 min. showed the air had reached the cecum. (C.) At 37 min., 2000 cc. of air in and flatus was being freely passed. (D.) At 110 min., there is relatively little of the gas left, flatus having been voluminously passed for 93 minutes.

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jects around the Levine tube, so that the amounts discussed are probably not entirely correct in all instances. This will be pointed out later by specific examples.

The roentgenograms for a typical experiment are shown in Fig. 5. This happens to be the subject in which oxygen was aspirated, but the results were the same for air. Roentgenogram B taken at 28 min., shows the wide general distribution and the distention produced by 1000 cc. of gas. Gas reached the cecum in 18 min., flatus was first passed at 36 min. and 800 cc. were collected in 74 min. Once started, the passage of flatus in this subject, as in others, was quite regular in time and amount, as would be expected by rhythmical peristaltic action. This is shown as follows:

Time of Passage: Minutes	Amount of Flatus: cc.
36	100
40	100
44	100
47	100
51	100
56	100
62	100
70	50
80	0
90	25
110	25
74	800

Fig. 6 shows the distention and rapid passage of 2000 cc. of aspirated air. Roentgenogram B is a good example of the distribution and distention produced by 1000 cc. Before 2000 cc. were ingested flatus was passing freely.

Fig. 7 shows the result of administering prostigmine methyl sulfate. The time for the gas to reach the cecum was no different than without prostigmine, and other subjects passed flatus just as rapidly. Actually prostigmine did not clear the bowel of gas. It is true that more flatus was passed than the known amount of air aspirated, but at 125 min. there is considerable gas in the stomach and colon and some in the small intestine. It is believed that the subject continued to aspirate air long after the Levine tube had been removed. The same result was obtained with this subject in a later similar experiment. He was a stoical individual and little disturbed by what went on around him. The prostigmine may have disturbed the intestines and produced a reflex resulting in the esophageal aspiration of air. It has been noted by others² that an enema may be followed by the rapid accumulation of gas in the small intestine and colon. The enema may quite possibly have disturbed the intestines and/or the patient in general with a resulting reflex aspiration of air. The nervous factor is commonly seen in gaseous distention.

The summary of the data, Table III, shows an average of 1133 cc. of air aspirated from the spirometer by the negative intra-esophageal pressures of moderately deep breathing in 30.4 minutes. At 20 respirations per minute

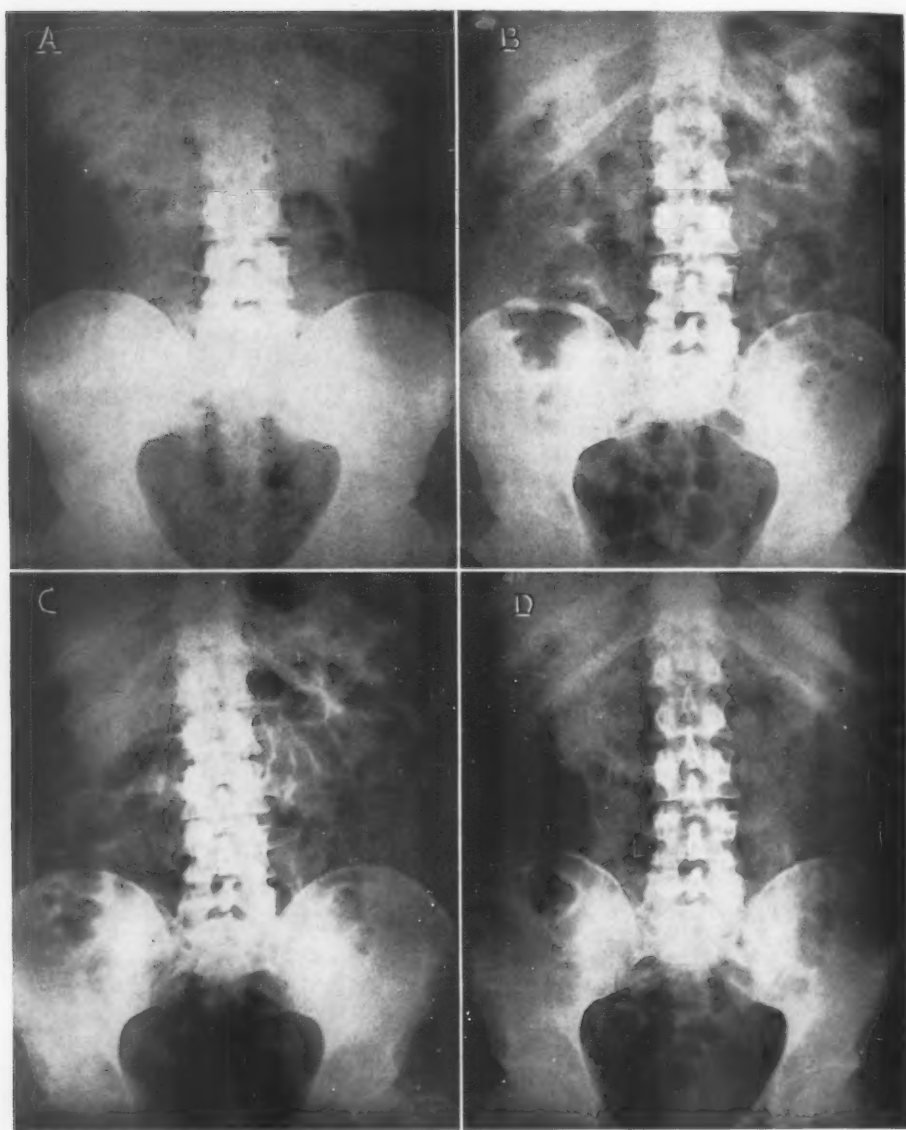


FIG. 7.—Roentgenograms showing effect of prostigmine on the passage of 1000 cc. of air. (V. T.¹) (A.) Initial film, 6 min. after the subcutaneous injection of 0.25 mg. of prostigmine methyl sulfate. Small amount of gas seen scattered throughout the stomach and bowel. (B.) At 25 min., 400 cc. of air aspirated and first flatus just passed. Intestinal distention appears too extensive for that amount. (C.) At 74 min., 1000 cc. of air in and 850 cc. of flatus passed. There is some gas in the stomach and considerable in the intestines. A second dose of 0.25 mg. of prostigmine was given when 1000 cc. of flatus had been passed. (D.) At 125 min., 1150 cc. of flatus collected, which is 150 cc. more than the amount of air aspirated from the spirometer. There is still considerable gas in the stomach and colon, and a small amount in the intestines. More air must have been aspirated than came down the Levine tube.

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this is roughly 2 cc. per inspiration. The average time of 14.6 minutes for the gas to reach the cecum compares fairly well with Magnusson's average of 10 minutes. His method of checking this time by a retained barium enema is probably more accurate. The objection may be raised that the enema might have increased intestinal peristalsis, but the Levine tube in the esophagus and the rectal tube might also have done the same thing. To avoid this possible irritation it is suggested that a small amount of radioactive argon gas be added to air injected into the stomach and its time appearance at the cecum and rectum determined by a Geiger counter.

The average time for the appearance of flatus was 24.1 minutes, which compares well with Magnusson's average of 30 minutes and is tremendously fast compared to the barium average of 18 to 24 hours. The average volume of flatus passed, 970.8 cc. in 83.6 minutes, was very close to the average of 1133 cc. of air aspirated.

This experiment corroborates Magnusson's finding on the rapid passage of ingested air through the gastro-intestinal tract, and accounts for gas

TABLE III.—*Summary of Data on the Rapid Passage of Air Through the Gastro-intestinal Tract*

Subject, and Age	Total Time Exp. Min.	Air Aspi- rated Into Esophagus Cc.	Min.	Approx. Time to Cecum Min.	Flatus		
					First App. Min.	Volume Passed Cc.	Time Passed Min.
NC	23	25	550	08	..	22
WH(1)	24	35	1650	30	..	24
WH(2)	24	125	2000	37	8	17
SC	24	64	1000	21	..	17	1025
RS	29	115	1000	33	16	25	600‡
LS(1)	23	165	1000	28	15	30	600‡
LS(2)	23	120	*1000	28	18	36	800
VT(1)†	28	105	1000	60	20	25	1150
VT(2)†	28	144	1000	29	12	19	1450
Average:			1133	30.4	14.6	24.1	970.8

* 100 percent oxygen aspirated from spirometer instead of air.

† 0.25 mg. of prostigmine methyl sulfate given subcutaneously immediately before experiment began and after 1000 cc. of flatus had been passed.

‡ Rectal tube clogged and flatus collection incomplete.

analyses showing the composition of intestinal gas to approximate with some reasonable modifications the composition of atmospheric air.

It is felt that a further investigation of air passage should be done when food or barium is taken at the same time. Patients with ileostomies, cecos-
tomies and colostomies could also be used as a check on the rapid passage of air. The influence of prostigmine and other drugs should be studied further.

METEORISM DURING PYELOGRAPHY

From the results of the previous study it is evident that gas seen roentgeno-
graphically in the ileum and colon may have entered the esophagus 10 to 20 minutes previously, and its possible origin as external air should be remem-
bered. The authors considered the accumulation of gas in the intestines

during pyelography as an example of the aspiration and quick transit of external air through the upper alimentary tract, and set out to prove the point.

The study of gastro-intestinal gas in patients undergoing intravenous or retrograde pyelography is a very appropriate experiment in many ways. The time period is short, about an hour. The increased amount of gas seen in many routine pyelographies is sufficient in amount to be measurable. The patient undergoes several possible uncomfortable and strange procedures which may be quite disturbing. With retrograde examination the urethra, bladder, ureters and renal pelvis are stimulated, a procedure often observed to be associated with and resulting in increased intestinal gas, even though

there is no pain.¹⁵ If one were to specify the conditions of the whole experiment they would be little different than the routine of a pyelography.

Method. The patients on whom the study was conducted were prepared in the usual manner for a pyelography.* No breakfast was allowed, and fluids were restricted for several hours before the retrograde, but not before the intravenous study. A few minutes prior to the initial pyelogram a Wangenstein tube was passed to the stomach and continuous suction started with water siphonage. By water displacement in a graduated collecting system the total amount of gas aspirated could be learned and individual volumes down to 0.25 cc. determined. The stomach was emptied of fluid and gas and the initial pyelogram made to determine the intestinal gas present at the onset. The patients were asked not to swallow. A careful record was then kept of the return of gas as related to the procedure of the

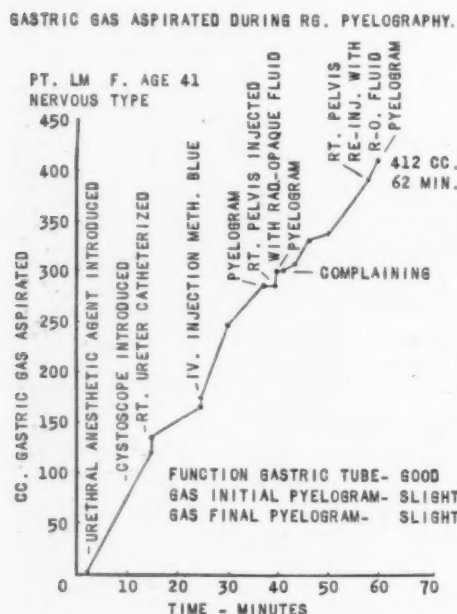


FIG. 8.—Record of gastric gas aspirated during retrograde pyelography in a nervous patient, L. M. Note the sharply increased gaseous return when the right ureter was catheterized, methylene blue was injected intravenously and the right renal pelvis was injected with the radio-opaque fluid. Respirations were increased in rate and depth at these times. Even roentgenographic exposures elicited a response.

pyelography, swallowing movements, complaints of the patient, changes in the rate and depth of respirations and any other emotional reaction. The pyelograms were utilized to determine the effectiveness of the gastric suction in keeping the stomach free or air.

Results. Fig. 8 shows a typical response in a nervous patient undergoing

* This part of the study assisted by Dr. Earl Barth, and Dr. V. J. O'Connor, Prof. and Chairman of the Dept. of Urology, Northwestern University Medical School.

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retrograde pyelography. In 62 minutes a total of 412 cc. of gas, roughly 7 cc. per minute, was aspirated from the stomach, and the process seemed definitely related to deeper and irregular respirations as nervous responses associated with the various procedures done, such as the passage of the cystoscope, etc. Of special interest was the fact that the stomach was kept empty of air and consequently there was no increase in intestinal gas from the initial to the final pyelogram. This is shown in Fig. 9. There is no evidence that the various procedures of the pyelography produced atony of the bowel and consequent expansion of gas already present, as suggested by Oppenheimer,¹⁵ or rapid diffusion of nitrogen into the bowel, as theorized by Begg.¹⁶

A second typical result in a nervous patient undergoing intravenous pyelography is shown in Fig. 10. This man had a total of 1345 cc. of gastric gas return in 64 minutes or roughly 20 cc. per minute, which is the largest

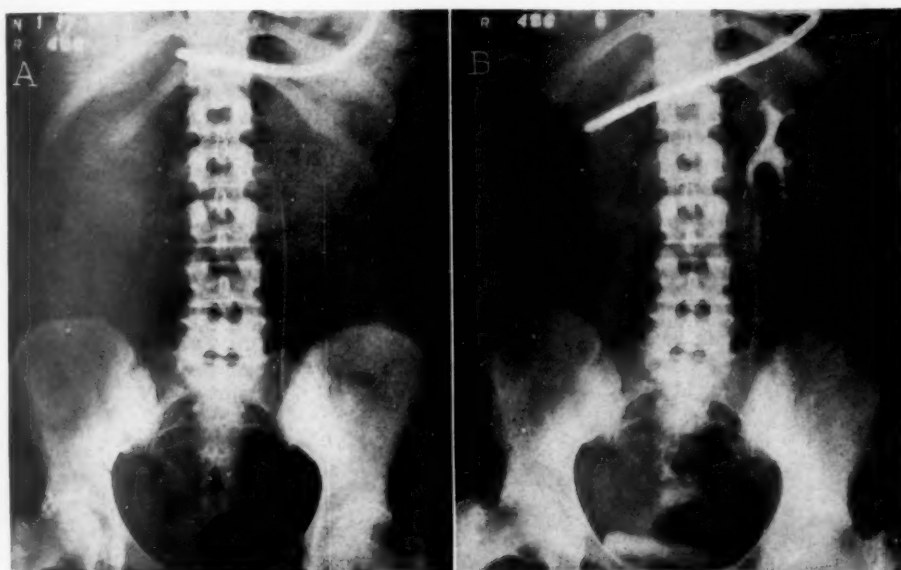


FIG. 9.—Roentgenograms of patient, L. M., who had 412 cc. of gastric gas aspirated during the 62 minutes of the retrograde pyelography. No increase in intestinal gas from the initial "A" to the final "B" roentgenogram because the stomach was kept empty of air.

amount obtained from the group studied. He swallowed infrequently, there was no visible air-sucking, aerophagy or belching, yet a steady amount of air passed down the esophagus and was aspirated from the stomach during the disturbing period of the pyelography.

From the summarized data in Table 4 the following comments are most pertinent.

The time period of study varied from 35 to 68 minutes and the volume of gastric gas aspirated from 45 to 1345 cc. The age and the sex of the patients seemed to make no difference. Outstanding was the fact that when

the stomach was kept empty of gas by good function of the gastric tube there was no increase in the amount of intestinal gas from the initial to the final pyelogram. If diffusion or fermentation were important sources of gas in these cases this would not be true. The evidence is that gas seen in routine pyelograms comes from external air.

An analysis of the gas returned from patient J. M. undergoing pyelography, and subject V. T. was as follows:

	CO ₂	O ₂	N ₂
J. M. (I. V. pyelography).....	1.70%	19.53%	78.80%
V. T.* (Deep breathing).....	7.57%	17.08%	75.40%
V. T.† (Air sucking).....	1.45%	19.46%	79.09%
City air.....	0.10%	20.85%	79.05%

V. T. 20 min. deep breathing—270 cc.
V. T.† 2 min. air sucking—700 cc.

J. M.'s concentrations are quite close to that of atmospheric air and compare well with the sample from V. T. who took in air by deep breathing and air-sucking. The higher values for carbon dioxides are possibly due to the known rather rapid diffusion of this gas into the stomach.¹⁸ Further gas analyses are being planned in a continuation of these studies.

GASTRIC GAS ASPIRATED DURING IV. PYELOGRAPHY.

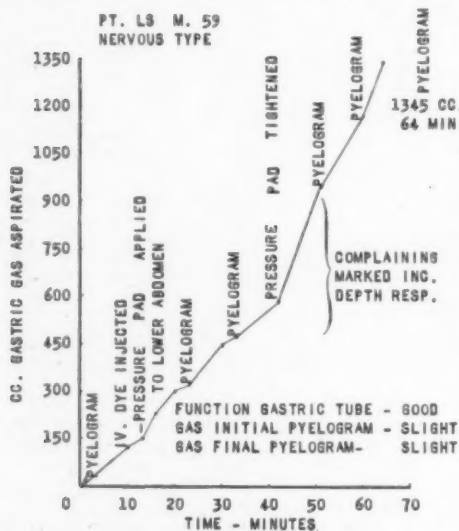


FIG. 10.—Record of the largest amount of gastric gas aspirated during a pyelography. L. S. was a very nervous patient. As noted for patient L. M. of Fig. 8, the various stimuli from the procedures carried out resulted in a marked increase in the depth and rate of respirations. This was accompanied by the most rapid gas return, the amounts aspirated per deep breath or swallow being greatest with this patient, averaging close to 5 cc. The discomfort from the lower abdominal pressure pad was the most disturbing factor.

When the function of the gastric tube by the observation of M. T. was only fair (two cases) or poor (five cases) there was an increase in gastro-intestinal gas from the initial to the final pyelogram. This (shown in Table 4) is indirect evidence that such gas comes from the outside, because it was there through failure to keep the stomach empty.

An important observation was that three times as much gas returned from the nervous patients than from the calm ones, the averages of Table 4 showing this distinctly, with no material variation whether the patients were undergoing intravenous or retrograde pyelography. This nervous factor is apparent in many observations on air entering the gastro-intestinal tract. Small amounts of gas were aspirated from the calm patients under even normal respirations and more with their few episodes of deeper respira-

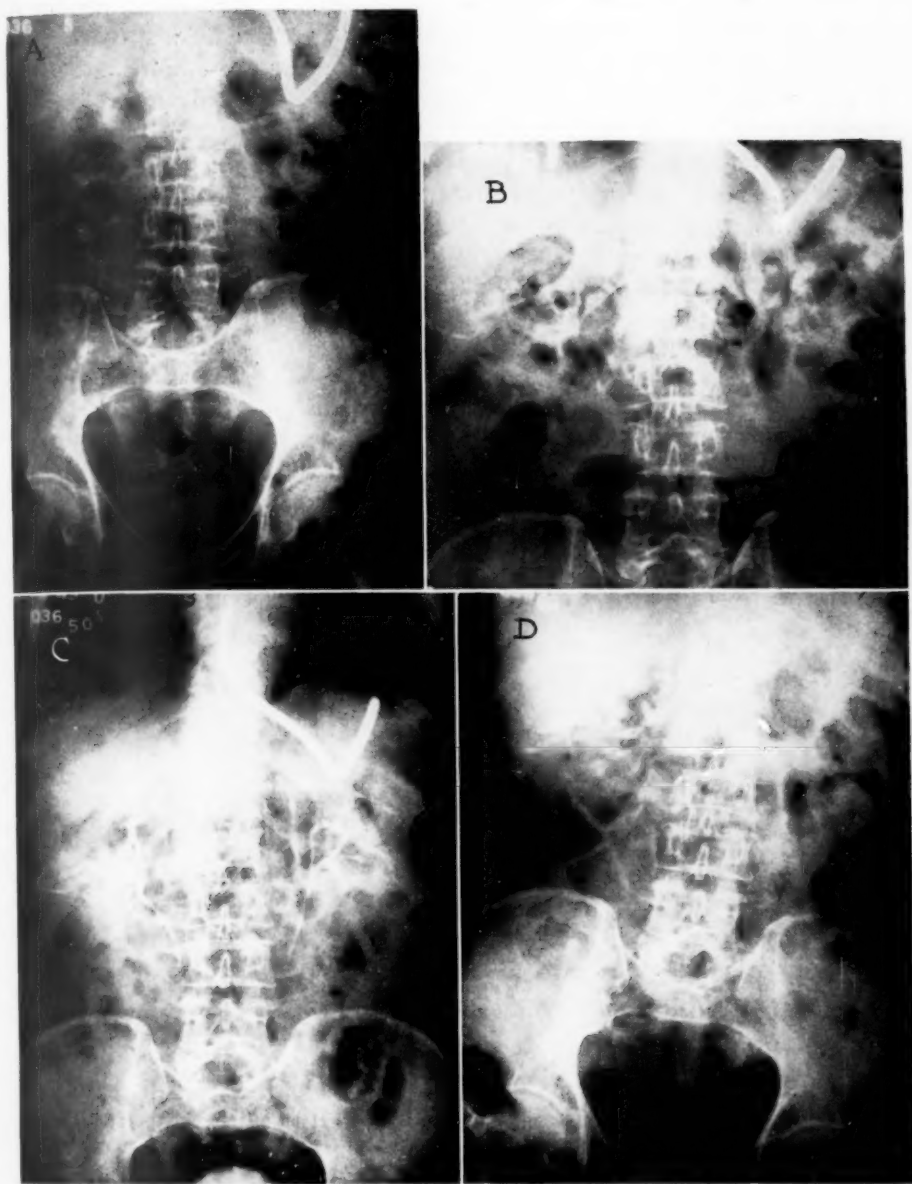


FIG. 11.—Roentgenograms of nervous patient, L. S., who had 1345 cc. of gastric gas aspirated during the 64 minutes of the intravenous pyelography. (A.) The initial film, just after the Levine tube had been inserted, shows a moderate amount of gas in the stomach and intestines. (B.) Twenty minutes after the intravenous dye injection, 460 cc. of gas aspirated. At least the stomach is empty. (C.) Fifty minutes after the dye injection, 1175 cc. of gas aspirated. Intestinal gas seems a little less than in A and B. (D.) Sixty minutes after the dye injection a total of 1345 cc. of gas had been aspirated. Six minutes before this film was taken the gastric tube was removed and gas is now seen in the stomach. The rapid ingestion of air is evident.

tions. The nervous patients were much more distressed, had longer periods of deeper breathing and consequently took in much more air. Two patients, E. S. and R. J., were addicted to frequent unconscious swallowing. This became pronounced during periods of distress and was likely responsible for much of the gas collected. The others by request were able to control the act of swallowing and in them this occurred too infrequently to account for any appreciable portion of the gas obtained.

The volume of gaseous return following a single swallow varied from 0.3 to 5.0 cc., averaging from 2 to 3 cc. Amounts of gas returned with one deep breath varied from 0 to 5 cc., averaging from 1 to 2 cc. A respiratory rate of 20 per minute gave plenty of opportunity to take in considerable air.

TABLE IV.—*Summary of Data on Gastric Gas Aspirated from Patients Undergoing Pyelography*

Subject, Sex and Age			Reaction of Patient	Gastric Gas Aspir.		Estimation of G-I. Gas On Pyelogram		Function Gastric Tube
				Min.	Cc.	Initial	Final	
Intravenous Procedure								
JW	M	53	Calm	61	100	Slight	Slight	Good
SB	F	68	Calm	62	105	Slight	Slight	Good
CB	F	44	Calm	52	195	Slight	Slight	Good
JA	M	51	Calm	46	45	Slight	Moderate	Poor
CS	F	42	Calm	61	165	Moderate	Moderate	Poor
FS	F	66	Nervous	37	165	Slight	Slight	Good
ME	F	53	Nervous	35	195	Slight	Slight	Good
RL	M	15	Nervous	44	200	Slight	Slight	Good
LW	F	43	Nervous	41	240	Slight	Slight	Good
LS	M	59	Nervous	64	1345	Slight	Slight	Good
PR	F	66	Nervous	68	280	Moderate	Moderate	Fair
RJ	M	23	Nervous	53	415	Moderate	Moderate	Fair
RB	F	18	Nervous	48	75	Slight	Moderate	Poor
ES	F	66	Nervous	50	175	Slight	Moderate	Poor
			Average Calm Group	56	122			
			Average Nervous					
			Group	49	343			
Retrograde Procedure								
DB	F	38	Calm	60	55	Slight	Slight	Good
MR	F	47	Calm	56	115	Slight	Slight	Good
WB	F	72	Nervous	40	225	Slight	Slight	Good
LM	F	41	Nervous	62	412	Slight	Slight	Good
PD	F	66	Nervous	45	90	Slight	Moderate	Poor
			Average Calm Group	58	85			
			Average Nervous					
			Group	49	242			

Important Findings: 1. Approximately three times more air aspirated from the stomachs of nervous patients than from the calm ones. 2. When the stomach was kept free of air by continuous suction through the gastric tube there was no increase in intestinal gas from the initial to the final pyelogram.

SUMMARY

There is nothing new in the idea that external air enters the esophagus under many conditions and is the major source of gastro-intestinal gas. It appears in the upper alimentary tract of infants within 15 minutes after birth¹⁹ and the roentgenographic findings of air in the bowel has been suggested as a test for extra-uterine life.²⁰

Normally the superior esophageal sphincter keeps the esophagus closed. With swallowing movements the sphincter relaxes and air enters with fluid and food. In the upright position the air collects at the top of the stomach, and when more than the usual amount accumulates, as with a meal, it is belched up. Alvarez² remarked that hundreds of patients can be examined with the fluoroscope before finding one with enough air in the stomach to be worthy of special comment.

Excessive amounts of air may enter the stomach by frequent swallowing, and also by the following methods which are variations of the same procedure. The air-sucker can consciously relax the superior esophageal sphincter and by attempting to breathe against a closed glottis can inspire or aspirate air into the esophagus, from which it passes into the stomach. The aerophagic is a nervous individual who unconsciously does the same thing and usually must be convinced of what he is doing to be cured of the habit. The laryngectomized patient can learn esophageal speech with air aspirated into the esophagus by the same method as that of the air-sucker. With skill his aspirations occur with almost normal inspirations and are practically unnoticeable. The repeated belcher takes air into the esophagus to belch with by the same method as the air-sucker, and some can say a few words with the eructated air in the same manner as the esophageal speech patient.

This study has shown that appreciable volumes of air enter the stomach by repeated belching. In the upright position the air is trapped in the cardia and nothing more disturbing than further eructations result, but when lying in bed the air may pass on and cause trouble. A patient with marked gastrointestinal distention from repeated belching is reported.

Patients undergoing anesthesia and operation were found to swallow infrequently, and little gas was aspirated from the stomach of the majority studied. One patient breathing against a partially obstructed airway took in a large amount of air during the operation. This is essentially inspiring against a closed glottis, as done by the air-sucker, and some relaxation of the superior esophageal sphincter by the anesthetic probably played a part. Considerable gas was aspirated from the stomachs of five patients during an operation under cyclopropane anesthesia plus curare. Each was considered to have a partial paralysis of the respiratory muscles due to the curare and positive pressure anesthesia was used. With curare the superior esophageal sphincter was probably well relaxed and the positive pressure forced gas into the stomach.

A rare case of massive, spontaneous pneumoperitoneum is reported. This resulted from perforation of the stomach which became tremendously dilated during a minor operation under sodium pentothal anesthesia. Those in the operating room heard the air entering the esophagus with each inspiration.

Air was found to pass very rapidly through the gastro-intestinal tract. Volumes aspirated into the stomach of experimental subjects reached the cecum in an average of 14.6 minutes and was passed as flatus in 30 minutes.

Oxygen passed along in the same rapid manner. It is evident that gas seen in the intestines on a roentgenogram may be largely atmospheric air which was aspirated esophageally a few minutes previously.

An excellent opportunity for studying rapid accumulations of intestinal gas was offered by patients undergoing pyelography. By continuous gastric suction considerable volumes of air were aspirated from the stomach, and when it was kept empty no increase in intestinal gas occurred. This is further evidence that external air is a major source of gastro-intestinal gas.

The nervous patients undergoing pyelography had three times as much air aspirated from their stomachs as the calm patients. The nervous manifestations were elicited mainly by intravenous injections, the passage of the cystoscope and ureteral catheters, the introduction of fluid into the renal pelvis, and the discomfort of the lower abdominal pressure pad. These stimuli resulted in increases in the depth of respiration, and the gas return was greatest during these periods. A previous study of normal subjects showed that increased depth of respirations increased negative intra-esophageal pressure, and consequently the rate of aspiration of air into the esophagus.

The finding that continuous gastric suction prevented the meteorism of pyelography is the same as continuous gastric suction preventing post-operative distention. Under both conditions considerable volumes of atmospheric air must enter the esophagus and stomach. We consider many patients thus become "temporary aerophagics," using the word in a broad sense. Marked aerophagia is usually a readily apparent, nervous phenomenon, but it can be a less evident process such as used by the esophageal speech expert. There is every reason to believe that patients under many conditions become temporary aerophagics and the stimulus may be entirely nervous without organic origin or be associated with an organic disease or injury and its treatment.

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DISCUSSION.—DR. WILLIS D. GATCH, Indianapolis, Ind.: This fascinating work of Dr. Maddock and his associates is of great clinical value. The ingestion of air is a common cause of symptoms diagnosed as gallbladder disease, ulcer, appendicitis, etc. A careful history will in most cases determine the diagnosis.

I have shown that extreme dilatation of the stomach of a dog will kill it in about two hours by asphyxia. I have observed acute dilatation of the stomach occur suddenly in hysterical patients. I remember two of these who would certainly have died had their stomachs not been deflated.

Air ingestion is, I think, an occasional cause of death under anesthesia.

I fully believe in what Dr. Maddock has said about the mechanism by which air gets into the esophagus, but I believe another mechanism acts in some cases. Perhaps Dr. Maddock has discussed this in his paper submitted for publication.

I derived by inference the following ideas from an article by Sir Arthur Keith published in 1913 in the *British Journal of Anatomy and Physiology*. This gives the best account I have ever found of the evolution of the diaphragm and its relation to the mammalian lungs. In the reptiles the lungs are in the abdomen. The great activity of which these creatures are capable proves that they must have a very efficient respiration such as could be carried on only by the continuous alternation of negative and positive pressure within the abdomen.

I believe that when the following events occur a negative intraabdominal pressure may be produced in man:

1. Contraction of the abdominal muscles.
2. Relaxation of the diaphragm. (The abdomen and chest then become a single cavity as far as pressure is concerned.)
3. Elevation of the ribs. (Under these conditions this creates a negative pressure in the abdomen.)
4. Relaxation of the superior sphincter of the esophagus.

A great quantity of air can then rush into the stomach. Some men can voluntarily perform these acts. This explains, I think, the trick of downing a bottle of beer at one gulp.

DR. JOHN RANDOLPH PAINE, Buffalo, N. Y.: Gentlemen, I believe Dr. Maddock has shown us very well how in many of our patients troublesome accumulations of gas occur, yet to my mind why these patients get gas accumulation seems a little mysterious.

To say that it is on some type of a nervous or psychogenic basis does not entirely satisfy me. It might be that some of us have received the impression that we need a psychiatrist to take care of the situation.

It would be nice, I think, if we could say beforehand that this patient will not be troubled with distention after operation, that this other patient will be so troubled; but I don't believe many or any of us can do that. I say this because, despite the fact that a surgeon in a small midwestern city once said that the institution of gastric duodenal intubation had made a civilized business out of abdominal surgery, still the more or less routine institution of gastric duodenal aspiration is not certainly all we might like to have it. Many of our patients complain of the discomfort of the tube, and usually the highstrung, nervous patient who complains is the very one who needs it most.

I think it is very evident that there are two elements here, one, a somewhat active element in which the patient, by swallowing air or air sucking, actively forces air into his stomach; but there is another element, another more or less passive element, in which by the rhythmic change of pressure in the chest, with respiration, air is pulled into the esophagus to be passed on down into the stomach.

I think these studies can be followed further with a great deal of profit. There would be two things I would be particularly interested in. One thing in which I am interested is to note what, if any, effect there is on accumulation of air in the gastrointestinal tract from the ingestion of various types of food. All of us know that certain types of food bother us more than other types.

Another thing is the question of why we don't have as much trouble as we might think we would have in patients in whom the stomach has been more or less denervated and pulled up into the chest. One would think if air were aspirated into the esophagus it could be aspirated as well into the stomach, and we should have a great deal of trouble with patients after esophageal resections; yet in my experience, somewhat limited, to be sure, trouble of this nature has not been very great.

However, some experiments in dogs leads me to think that occasionally this is a very serious problem. At numerous times we have denervated the stomach freely from its attachment in the abdomen and pulled it into the chest. Most of those dogs die within two weeks; some of them die within two or three days and some within 24 hours from an acute dilatation of the stomach. I have seen one dog go as long as six weeks, be perfectly all right, and within five minutes after apparently being perfectly all right, be dead. At autopsy the chest was opened and the stomach was tremendously distended with gas.

These accumulations can occur from some mysterious cause, as far as I know, in a very short time.

DR. WALTER G. MADDOCK, Chicago: I wish to thank Drs. Gatch and Paine for their remarks. They have long been interested in abdominal distention and their suggestions will be investigated.

We have planned considerably more work on this problem. We know that in allergy patients certain foods will cause rapid distention, and such a phenomenon offers an excellent opportunity to learn more of the mechanism of gas entrance into the upper gastro-intestinal tract. We have been impressed by the nervous element in many instances of gastro-intestinal distention. For instance, during pyelography the amount of gas taken in by the nervous patients was three times more than for the calm patients. Surgeons have occasionally been able to predict a stormy postoperative course because a patient was extremely nervous and apprehensive, and therefore was

GASTRO-INTESTINAL GAS

easily upset by the operation and subsequent care, was unable to void and developed marked gaseous distention, all leading to a poor convalescence.

In regard to the rapid passage of air through the gastro-intestinal tract we believe the studies should be repeated when food or barium are taken at the same time as the air. This may not be important clinically because many patients during the period of distention are eating lightly or not at all. The effect of various drugs on the rapid passage of air should also be investigated. I would like to add a radio-active gas as a marker for the passage of air through the alimentary canal. Further information on the time of passage might be obtained; and in tune with the times, all modern experiments employ a radio-active substance and a Geiger counter.

Dr. Paine's observations on patients whose stomach has been brought up into the chest and his work on dogs along this line are interesting. Considering the possibilities of negative intra-gastric pressure from thoracic respiratory movements these patients should certainly have some trouble. Dr. Richard Sweet's observations are the same as Dr. Paine's in that during the immediate postoperative period there is often some distention, but this subsides in a few days' time.

Dr. Gatch's remarks about the men who can drink a bottle of beer without swallowing are pertinent because these individuals are examples of those who can voluntarily open the superior esophageal constrictor without swallowing. I would like to call on one of my co-authors to come up here for a moment. He can voluntarily relax the superior esophageal sphincter and will give a demonstration of air sucking and belching. Notice how he moves the chin forward as part of the process of relaxing the sphincter. Then by attempting to draw in a breath against a closed glottis he is able to aspirate air into the esophagus, and a good belch follows.

I am sure the members of this organization have seen many instances of distention occurring with grunting or exaggerated respirations from a variety of causes. We well know that the effects of distention are serious and often are lethal. It is fortunate that we have learned the value of continuous gastric suction and one cannot over-emphasize that our efforts should be directed towards preventing distention rather than having to treat it after it has occurred.

SPHINCTER PRESERVING OPERATIONS FOR RECTAL CARCINOMA AS RELATED TO THE ANATOMY OF THE LYMPHATICS*

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ALL SURGEONS interested in the management of carcinoma of the rectum, rectosigmoid and lower sigmoid are mindful of a slowly changing trend from the radical abdominoperineal resection with complete extirpation of the sphincter apparatus to a radical procedure with preservation of the sphincter mechanism. This is a revival of the ambition of all the early surgeons who conservatively removed the malignant growth but saved the posterior stoma of the gastrointestinal tract with hopes of proper control of this orifice. Because of our unending efforts to improve the management of disturbances of the human body, the pendulums of thought and action keep swinging, usually toward progress and better goals. Occasionally something entirely new makes its appearance, but more frequently the new thought or mode of execution is an elaboration and popularization of material introduced by our predecessors. Usually, with each revival, something constructive evolves; the pattern of management or treatment may change in entirety or only in part, or it may possibly retain the status quo.

Today we are fervently discussing all the aspects of the proper treatment of carcinoma of the rectal and rectosigmoidal areas. Some hesitate to return to a discussion of any operative procedure which entails an attempt to preserve the sphincter mechanism because of the poor results experienced prior to the introduction of the popular radical abdominoperineal procedure (so-called Miles operation) of the last 25 years. However, we must not forget that some of the same forces which have worked to improve our results with this procedure may also be of assistance in some slightly less radical procedure which does not destroy the controlling outlet of the lower intestinal tract.

Usually our discussions deal with the local anatomy of the lymphatics. However, other factors must be considered when one discusses recurrence of malignant growths. Carcinoma spreads by direct extension, by venous channels, by the lymphatic channels and by transplantation, and all these avenues of spread should be kept in mind when considering recurrence of rectal carcinoma following various operative procedures.

Our surgical principles for removal of malignant growths demand that we excise widely from the palpable tumor margins. In carcinoma of the rectum, the intramural spread or extension downward in the rectal wall has been

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investigated frequently, and it is most unusual to find tumor cells $2\frac{1}{2}$ cm. (1 inch) below the palpable tumor margin. One is referred to the studies of McVay,¹⁸ Gilchrist and David¹⁴ and Collier, Kay and McIntyre.¹⁰ Thus, if one transects the rectum 4 to 5 cm. ($1\frac{1}{2}$ to 2 inches) below the palpable tumor margin, there need be little fear of local recurrence from this factor.

The dissemination of cancer cells through the blood stream does occur, but references to this in the literature are relatively few. Perhaps more emphasis should be placed on this potentiality. In carcinoma of the rectum, the findings of inoperability and recurrence are most frequently coincident with the presence of malignant cells in the liver or in the general peritoneal cavity. Again, not infrequently, we find a relatively small rectal lesion, or a large rectal lesion with no involvement of adjacent lymph nodes, and yet we discover diffuse metastatic nodules in the liver. The route of vein invasion of small tributaries of the portal system and dissemination in the liver is certainly more direct than the passage through lymph channels, the thoracic duct, and then into the general venous circulation. Brown and Warren⁸ found vein invasion in 61 per cent of 165 autopsies on patients with rectal carcinoma. Grinnell,¹⁷ in a series of 75 fresh surgical specimens of carcinoma of the rectum, found the incidence of blood vessel invasion to be 36 per cent. One cannot help but be impressed by those instances where there is no macroscopic or microscopic evidence of lymph node involvement and yet signs of early recurrence are ushered in by liver metastasis. It is doubtful that removal of a sphincter area which is a reasonable distance below the tumor margin would alter the percentage of recurrences if vein invasion is a factor. This danger would be centripetal.

Since so much has been written on spread of carcinoma through the lymphatics, and such great emphasis has been placed on the radical excision of tissues above and lateral to the tumor and even on excision of the remaining anus and rectum to conform to the principles of the Miles procedure in carcinoma of the rectum, a careful review and careful analysis of all the facts should be made. The anatomy of the lymphatics has not changed but our concept of the mechanics or physiology may change. There is no controversy about the zone of upward spread but the zones of downward and lateral spread should be re-evaluated.

Unfortunately, little attention was given to the report of McVay¹⁸ in 1922 on the involvement of lymph nodes in 100 cases of carcinoma of the rectum. Although 47 had metastasis to lymph nodes, in only one case was there involvement of a lymph node below the lower margin of the lesion, and this was at the 1 cm. distance. Since then other reports on node involvement below the lower margin of a tumor have been made by Wood and Wilkie²¹ in 1933, Westhuer²⁰ in 1934, Gabriel, Dukes and Bussey¹³ in 1935, Gilchrist and David¹⁴ in 1938, Collier, Kay and McIntyre¹⁰ in 1940, Grinnell¹⁷ in 1942, and Glover and Waugh¹⁶ in 1944. In analyzing the reports on downward spread, we find only five cases (.8 per cent) of the total of 607 cases reported in which there was

lymph node involvement more than 2 cm. below the lower margin of the tumor (Table I). The significance of this low percentage as balanced against the number of patients in this group who actually died of recurrent cancer within the five year period cannot be denied. In this latter group, an estimate of 200 or approximately $33\frac{1}{3}$ per cent would be conservative. At this time, and from these figures, one cannot authoritatively debate that transection of the rectum 5 cm. (2 inches) below the lower margin of the lesion following radical excision above and lateral to the incision would have seriously altered the percentage of cures. It is possible that actual experience may at some time prove, because of factors unknown at this time, that it is more feasible to remove the anorectal segment. Such evidence is not available at this time under modern surgical conditions and technic.

TABLE I.—*Collected Data on Incidence of Lymph Node Involvement Below Margins of Malignant Lesions.*

Author	Year	Cases Studied	Cases with Nodes (1 to 2 cm. below lesion)	Cases with Nodes (2 cm. or more below lesion)
McVay.....	1922	100	1	0
Wood and Wilkie.....	1933	100	0	0
Westhuer.....	1934	74	1	0
Gabriel, Dukes and Bussey....	1935	100	2	0
Gilchrist and David.....	1938	25	0	2
Collar, Kay and MacIntyre....	1940	33	1	0
Grinnell.....	1942	75	1	0
Glover and Waugh.....	1944	100	6	3
Total cases.....		607	12	5
Percentage.....			2.3	.82

Lateral spread is a factor which probably is not so clearly understood because it is possible that our surgical specimens have not been excised widely enough in this direction and thereby are not permitting a true analysis. This must be particularly true in lesions of the mid- and lower rectum adjacent to the levator ani structures. Gilchrist and David¹⁴ noted lateral spread in four of 47 surgical specimens, or 8.5 per cent. Coller, Kay and McIntyre¹⁰ found lateral spread in six of 53 surgical specimens, or 11.3 per cent. Because of this rather vague understanding of the lymphatics of the levator ani muscle and fascia and the lymphatics above and below the levator ani muscle, a study of these structures was undertaken several years ago. After preliminary experimentation with various substances to demonstrate lymphatic patterns, the one we chose to use most frequently was India ink neutralized to pH 7.2 with n/10 hydrochloric acid suspended in an equal volume of isotonic saline. A 2 cc. syringe with a 27-gauge needle served as the instrument for injecting the dye material into the lymphatics. The dye was injected slowly under constant minimal pressure and the quantity used never exceeded 0.2 cc. in any given area of tissue. The first studies were made in animals and final studies

were completed on 15 stillborn fetuses. The details of the experiments are being reported in a thesis on the subject.⁷

After a careful review of previous studies on this subject and a careful analysis of our material, we have in our own minds crystallized the pattern for the lymphatics of the anorectal area with particular reference to the anal canal and the rectum adjacent to the levator ani muscle. There is a lymphatic network in the perianal skin, including the lower anal canal to the level of the mucocutaneous junction, and another lymphatic network in the remaining anorectal mucosa and rectal wall structures. These lymphatic plexuses are drained by three groups of efferent channels identified as the inferior, middle and superior channels draining corresponding areas of the anorectal canal (Fig. 1).

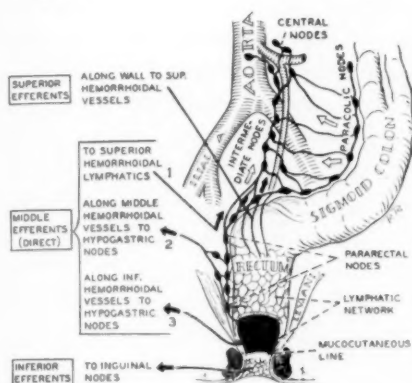


FIG. 1

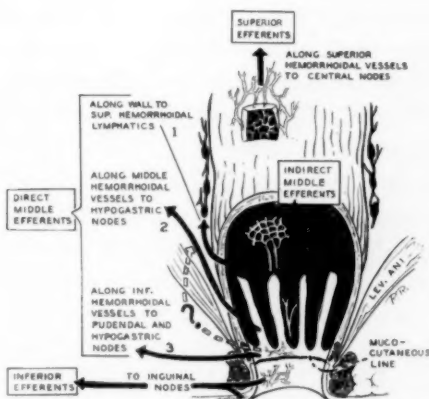


FIG. 2

FIG. 1.—Diagram of the lymphatic pattern for the anus, rectum, and rectosigmoid region.

FIG. 2.—A more detailed diagram of the lymphatics of the mid and lower rectal region, i.e., that segment of rectal wall adjacent to the levator ani muscles.

The inferior efferent channels drain the immediate perianal region and the anal canal to the level of the mucocutaneous line. Frequently two or three small efferent lymphatic channels were demonstrated on either side leading along the perineum or medial aspect of the thigh and emptying into the superficial inguinal lymph nodes. From this study, it would be interpreted that with an epithelioma in the perianal region which did not involve the true anal canal, lymphatic spread would occur only to the inguinal lymph nodes. Treatment with radium would probably suffice, although radiation or inguinal lymph node dissection should be considered. If the lesion is definitely within the anal canal and below the mucocutaneous line, similar management might be adequate, as our studies did not reveal communicating channels between the inferior and middle groups of lymphatics at the level of the mucocutaneous line. However, there is a possibility that the cancer might spread by break-through from the inferior to the middle group of lymphatics and then into the lymphatics on the under or upper surface of the levator ani muscles. With this possibility in

mind, a radical abdomino-perineal excision is indicated, with wide excision of the levator muscles and sacrifice of the sphincter mechanism.

The middle efferent channels drain the level at and above the mucocutaneous juncture and to or above the level of the middle hemorrhoidal vessels, particularly that part of the rectum which is attached to or adjacent to the levator ani muscles. These middle efferent channels are divided into the indirect and direct channels. The indirect channels ascend in the columns of Morgagni and continue upward into the lymphatic network of the upper rectal mucosa. The direct channels perforate the wall of the rectal canal and travel in three different directions. (1) Those in Group I are rather inconstant; they correspond to the course of the inferior hemorrhoidal vessels below the levator ani muscle and traverse the ischiorectal fossa, terminating in nodes along the internal pudendal vessels and thence to the hypogastric nodes along the internal iliac. Lymphatic channels perforating the levator ani muscle itself are practically non-existent as evidenced by our injections. In two instances, a single minute lymphatic channel pierced the levator muscle to apparently end in the hypogastric nodes. (2) Group II channels correspond to the course of the middle hemorrhoidal vessels, draining the area of rectum attached to or adjacent to the levator ani muscles. These channels lead to the hypogastric glands along the internal iliac vessels. (3) Group III channels perforate the rectal wall, ascend along the rectal wall into the pararectal nodes and thence upward along the superior hemorrhoidal vessels (Fig. 2). Carcinomatous lesions in the area of these middle efferent channels would include those lesions within approximately 10 cm. (4 inches) of the external sphincter margin, and above the mucocutaneous line. These lesions have good potentialities for lateral spread, but as previously stated Gilchrist and David¹⁴ reported only 8.5 per cent and Collier, Kay and McIntyre¹⁰ reported only 11.3 per cent from a careful study of fresh surgical specimens.

Balancing the apparent potentialities for lateral spread and the relatively small percentage reported against the general acceptance that lesions of the lower rectum give the poorer prognosis, there should be some attempted explanation. Dukes¹² has expressed the opinion that lesions in the mid-rectal region did less well than similar lesions elsewhere in the rectum because of the tendency of such lesions to grow laterally along the lymphatics accompanying the middle hemorrhoidal vessels. Gilchrist and David¹⁵ in 1947 reported that the five year survival rate for low lying carcinoma of the rectum (below peritoneal reflection) without evidence of gland involvement was 74.4 per cent, while the survival rate for lesions at or just above the peritoneal reflection was 90 per cent. Where nodal metastasis was present, the figures for similarly placed lesions were 37.5 per cent and 51.4 per cent. Waugh and Kirklin¹⁹ in 1949, in a somewhat similar analysis of their cases, reveal a 70.5 per cent five year survival rate in patients where no gland involvement was present and the lesion was below the 10 cm. (4 inch) level, and a 68.1 per cent survival rate with lesions at or above the 11 cm. level. Here, this difference is not

noticeable. However, when node metastasis was present, the five year survival rate for patients with lesions below the 10 cm. level was only 24 per cent and with lesions at or above the 11 cm. level, the figure was 33.3 per cent. The latter authors further analyzed the survival rate as related to the level of the lesion and revealed that the survival rate for the region between the 3 to 6 cm. level was only 17 per cent if metastasis was present. The lower five year survival rate for these lesions at the lower levels is further suggestive that in the area where the levator ani muscles are most closely associated with the rectum, the problem of complete extirpation of the malignancy is more complicated.

The investigations of Gilchrist and David,¹⁴ who studied fresh surgical specimens, clearing them by a modified Spalteholz technic, were a most careful study, and there was a 62 per cent lymph node involvement in their cases. Waugh and Kirkin¹⁹ studied old uncleared surgical specimens and there was only a 43.2 per cent node involvement; quite possibly their five year survival rate in cases with metastasis would be a little higher if they had examined the specimens in the fresh state by the clearing technic as node structures are better identified. In any event, their figures are of importance and are quite parallel. There is a noticeably poorer prognosis in lesions where the rectum is attached or adjacent to the levator ani muscles, and particularly when lymph node involvement has been demonstrated. From these survival rate figures of other authors for patients with or without lymph node involvement in lesions located above the mucocutaneous line and below the 10 cm. level, and from our experimental study of the lymphatics, it would seem that wider extirpation of the levator ani muscles, fascia and adjacent lymphatics is indicated. This cannot be accomplished by an operation where the dissection, resection and anastomosis are accomplished from within the abdomen. The proper procedure for lesions at these levels would appear to be that of abdominal dissection to assure sufficiently high extirpation, followed by posterior dissection and anastomosis to permit radical removal of the levator ani and adjacent structures.

The superior efferent collecting trunks were shown to pass through the muscular coat of the upper rectum and rectosigmoid area and extend backward and upward to reach the pararectal nodes and course upward along the superior hemorrhoidal vessels (Fig. 2). In carcinoma at this level (above 10 cm.) where the lesion is not directly adjacent to the levator ani structures, it would appear that transection of the rectum $3\frac{1}{2}$ to 5 cm. ($1\frac{1}{2}$ to 2 inches) below the lower margin of the tumor, wide excision laterally but not removing the levator structures, and adequate high transection of the sigmoid to eradicate paracolic nodes, should suffice.

One of us (R. R. B.), over a period of ten years, and only in selected cases, has done a radical excision of carcinoma of the rectosigmoid region with immediate anastomosis of the colon to the rectal stump, and on occasion has anastomosed the ileum to the rectal stump⁶ for carcinoma of the rectosigmoid. Beginning in 1946, in view of various publications on the subject

relative to the lymphatics, direct efforts have been made to preserve the sphincter mechanism, if at all feasible, in patients with carcinoma of the lower sigmoid, rectosigmoid or rectum. Of course, these sphincter preserving operations were done only when it was felt that a radical eradication of the disease was also being accomplished. The modified pull-through operation of Hochenegg, as advocated by Babcock¹ and Bacon,² was tried a few times, but our experiences were not satisfactory.

Gradually, three different operative procedures were developed³⁻⁵ and used where it seemed practicable to forego the radical abdomino-perineal excision of Miles and to attempt to preserve the sphincter mechanism. *Operation I* is entirely an abdominal operation, with radical excision of the sigmoid, rectosigmoid, and mid and upper rectum, for lesions at or above the 10 cm. (4 inch) level from the external margin of the anal canal, provided one is able to transect the rectum at least 3½ cm. below the lower margin of the lesion and effect an end-to-end anastomosis. In some of the earlier cases this operation included lesions 5 cm. (2 inches) from the anal sphincter, but with further experience, study and analysis, we felt these lower lesions should be attacked by a combined abdominal-perineal approach. *Operation II* is the combined abdominal-perineal procedure in which the dissection and freeing of the upper zones of spread are done from within the abdomen. Then the patient is turned onto the left side and further dissection and resection and the anastomosis are accomplished through a sacral incision. We now feel this operation is indicated in those lesions between the 5 cm. (2 inch) and 10 cm. (4 inch) levels. One cannot excise the levator muscle, fascia and the lymphatics on their upper and lower surfaces from within the abdomen; this is only accomplished through the posterior incision. Early in our investigative work on the lymphatics of the levator region, we became conscious that the operation for low and mid-rectal carcinoma was inadequate when executed entirely from within the abdomen and therefore we developed a technic for abdominal dissection, posterior resection and anastomosis. Also, we became more and more conscious that in the Miles operation of radical abdomino-perineal excision we were probably not being sufficiently radical in the excision of the levator muscles and adjacent structures in lesions below the 10 cm. level. *Operation III*, perineal dissection, resection and anastomosis, is accomplished entirely through the posterior approach. It is not a fundamentally sound operation for carcinoma of this area because one cannot adequately remove the zone of upward spread. However, it may be the operation of choice in some poor risk patients when the entire lesion is palpable per rectum (*i.e.* the upper level can be definitely determined), and in some other unusual circumstances. The lower margin of the tumor should be at least 2½ cm. (1 inch) above the upper margin of the muscular anal canal. This operation is similar to the Lockhart-Mummery procedure, except that the anus is not removed and an anastomosis is accomplished.

The last cause for recurrence of carcinoma in this region, as mentioned earlier in this paper, deserves some consideration. Carcinoma by transplant, either independently or as a factor in the operative procedure, must occur more frequently than is mentioned in the literature. That this complication occurs in the line of incision for breast carcinoma and in some abdominal incisions is well known. Recently, Chase⁹ emphasized that in operations for cancer of the breast, the carcinoma cells can frequently be found in stained smears made from gloves or instruments or centrifuged sediment from hand basins. The same must hold true when we divide any segment of the gastrointestinal tract. The recovery of malignant cells in this type of study would only be the application of the Papanicolaou principle for diagnosing malignancy in body secretions. This brings up the question of how long these detached

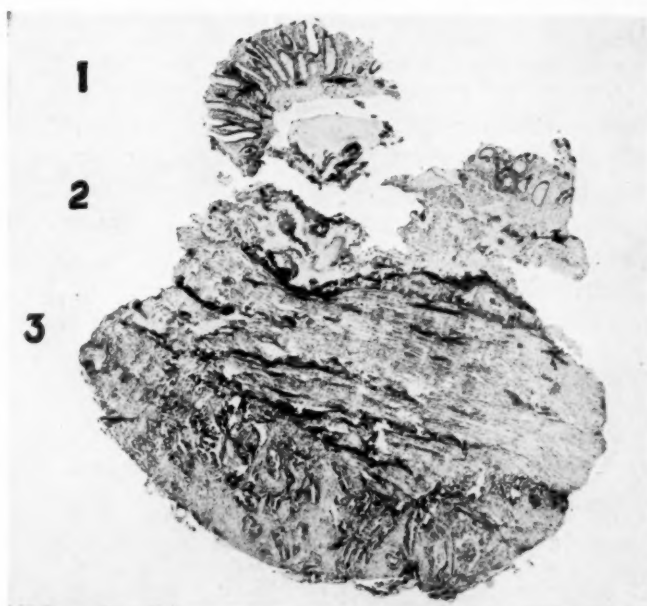


FIG. 3.—Microscopic section through tumor area in a patient with recurrent carcinoma of the rectum.

1. Normal mucosa was present.
2. The muscular layer of rectal wall was normal.
3. An extrarectal tumor mass of carcinoma was present.

carcinoma cells survive. One of us (R.R.B.) has had the opportunity to do an abdomino-perineal resection in one of our patients where recurrence had followed rectosigmoidectomy with anastomosis 13 months previously. In this patient, a mass developed in the hollow of the sacrum and, by palpation and visualization, the mucous membrane of the rectum appeared intact. A radical Miles operation was carried out, the fresh specimen was closely examined microscopically and macroscopically, and it was definitely established that the recurrence was a transplant growing between the sacrum and the rectal wall (Fig. 3). In a second case where recurrence was found, the mucosa at the

site of recurrence appeared normal, but at re-operation the lesion proved to be non-resectable and there was no final opportunity to prove or disprove the transplant phenomenon. The question of transplants in this area is of considerable concern to us and it is being further investigated.

In a series of 51 consecutive cases where preservation of the sphincter mechanism was given serious consideration, yet radical eradication of the malignancy was kept foremost in mind, we operated upon 44 patients, an-

TABLE II.—*Carcinoma of Rectum and Rectosigmoid; Analysis of 51 Consecutive Cases.*

	Cases	Operated*	Resected*	Anastomosis†	Abd-perineal†
Number.....	51	44	38	29	9
Percent.....	..	86.2%	74.5%	76.3%	23.6%

* Per cent of total cases seen. † Per cent of resectable cases.

Note: The percentage of anastomoses in resectable cases has decreased (88% of first 33 cases reported, 83.4% of first 40 cases reported, 76.3% of first 51 cases reported). The remaining resectable cases were treated by abd-perineal resection.

operability rate of 86.2 per cent. Thirty-eight (74.5 per cent) of these were resectable. In 29 patients, or 76.3 per cent of those resectable, a sphincter preserving operation was accomplished by one of the procedures we have elected to call Operations I, II and III. In nine cases (23.6 per cent), because of the low location of the lesion or some other factor, abdomino-perineal resection was done with sacrifice of the sphincter apparatus. In other words, we preserved the sphincter mechanism in 29 of the 38 resectable lesions (Table II). Among the resectable cases, there were two deaths, a mortality

TABLE III.—*Carcinoma of Rectum and Rectosigmoid; Mortality in 51 Consecutive Cases.*

	Cases	Operated	Resected	Anastomosis	Abd-perineal
Number.....	51	44	38	29	9
Per cent.....	..	86.2%	74.5%	76.3%	23.6%
Deaths.....	..	4*	2	2	0
Per cent.....	..	9.0%	5.2%	6.8%	0%

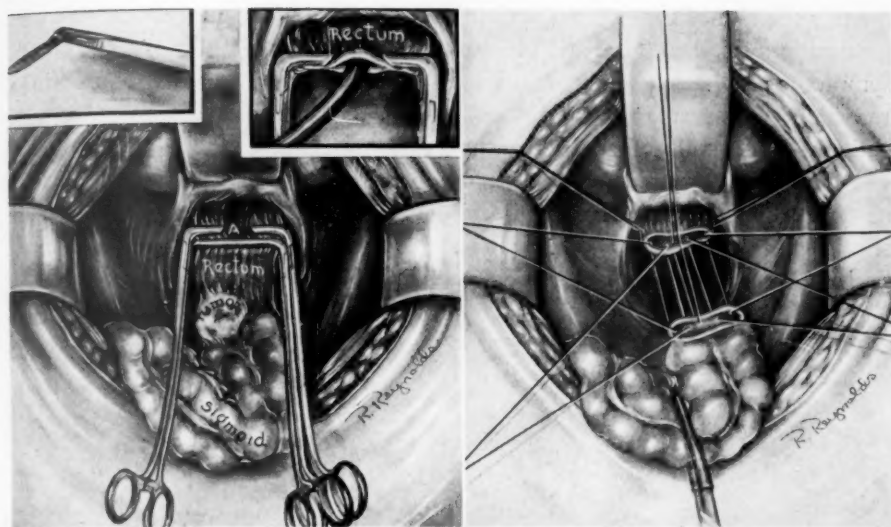
* Two of these deaths followed colostomies.

rate of 5.2 per cent for the 38 cases. These two deaths occurred in the group of 29 cases where an anastomosis was accomplished, giving a mortality rate of 6.8 per cent for rectosigmoidectomy with anastomosis. There were no deaths among the nine cases of abdomino-perineal resection (Table III).

At the present time, we have data on recurrences in three patients—one who has died and two who were re-operated. I have had the good fortune to re-examine and re-operate on these two patients. In one, the lesion was found to be so infiltrative throughout the pelvis that only a colostomy was done. In the other patient, an abdomino-perineal resection was accomplished.

Although time and further experience may prove some inadequacies of these sphincter preserving operations, one cannot help but be impressed by the probabilities of diagnosing recurrences in the pelvis far earlier than when the abdomino-perineal resection has been done. One is unable to examine ade-

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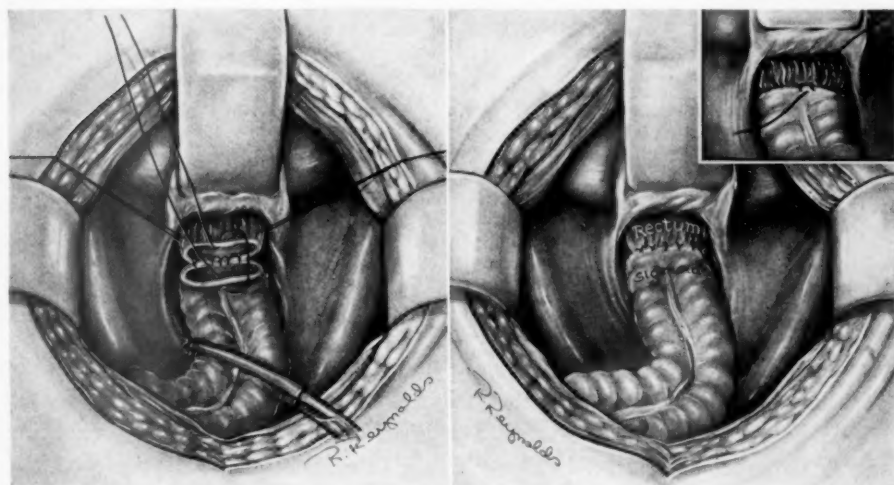


A

B

FIG. 4.—Anterior dissection, resection and anastomosis. (A.) Special clamps** applied below the tumor mass permit transection at least one inch below the tumor margin. Catheter suction introduced into lower segment between clamps removes contents. (B.) Short nosed lower clamps removed and replaced by guy sutures to steady lower segment. Five long posterior catgut guide sutures inserted to direct correct apposition of posterior walls; knots will be on mucosal side.

** By V. Mueller Company, Chicago, Illinois.



A

B

FIG. 5.—Anterior dissection, resection and anastomosis. (A.) The five posterior guide and inversion sutures have been tied. One similar inversion catgut suture is placed on the anterior wall, knot on mucosal side. (B.) The anastomosis is completed with a layer of figure of eight silk sutures on anterior and lateral walls and insofar as possible on the posterior wall. A penrose drain is placed in the hollow of the sacrum, peritoneum of pelvic floor is sutured over the drain and around the rectum. A Gibson type cecostomy is accomplished and after closure of abdomen, the patient is turned on the left side and the drain delivered posteriorly through a small incision alongside the coccyx.

quately the site of the original lesion following the Miles procedure, but with an anastomosis, the digital and proctoscopic examinations are still possible, and symptoms are expressed. In the one case where we did an abdomino-perineal resection 13 months following rectosigmoidectomy with anastomosis, the patient is well and active six months postoperatively.

There has not been a sufficient number of cases reported by a sufficient number of surgeons to permit definite conclusions from comparison of five year survival rates of patients who have been treated by radical abdomino-perineal excision and sacrifice of the sphincter, and of those who have had radical

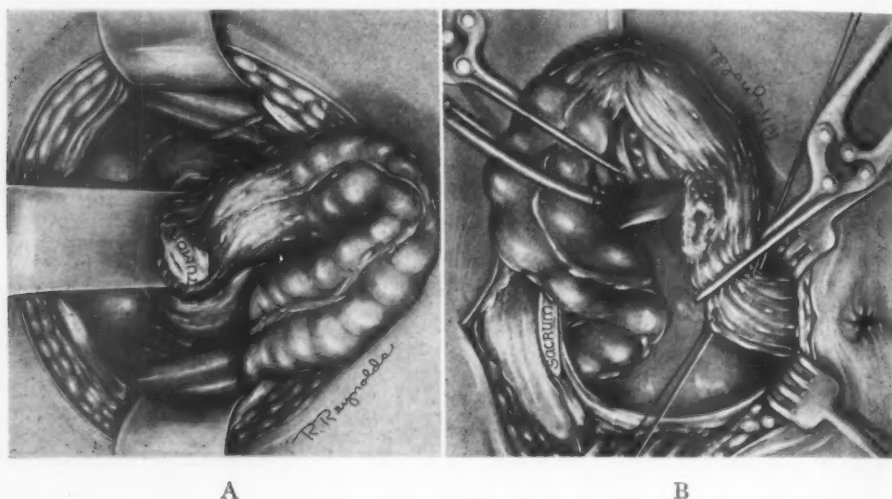


FIG. 6.—Anterior dissection with posterior resection and anastomosis. (A.) Through an abdominal incision, pelvic structures have been dissected and freed. The tumor mass which has been freed is replaced in the hollow of the sacrum and the pelvic floor peritoneum sutured around the rectum loosely enough to permit drawing the sigmoid downward through the posterior incision. A Gibson type cecostomy is accomplished and the abdomen closed. (B.) With the patient on his left side, an incision has been made along the coccyx and sacrum, coccyx is removed, wide dissection of levator ani structures is accomplished, and the rectum and sigmoid delivered and resected.

rectosigmoidectomy, anastomosis and preservation of the sphincter mechanism. This is particularly true when the lesion is below the rectosigmoid. In 1948, Dixon¹¹ reported to this Association on his experiences with anterior resection and anastomosis in selected cases. The greater percentage of these patients had lesions at the rectosigmoid and upper rectum, although some with lesions between the 6 and 10 cm. levels were reported. Of 272 patients, he reported a 57.7 per cent five year survival rate. Then Waugh¹⁹ in early 1949, in a paper discussing the importance of the level of the lesion in the prognosis for carcinoma of the rectum and low sigmoid, reported the five year survival rates of patients having adenocarcinoma of the rectum and low sigmoid colon treated by combined abdomino-perineal resection. In this report on 262 cases operated

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between 1931 and 1940 inclusive by different surgeons of the Mayo Clinic, the five year survival rate was 52.4 per cent. These lesions were above the 6 cm. level, similar to those reported by Dixon. This is most difficult for those surgeons who are strong advocates of the Miles procedure in all cases of rectal carcinoma to appreciate, or for the surgeon who believes the sphincter preserving operation is only indicated in selected cases, because the five year survival rate is better in the group where a sphincter preserving procedure was accomplished. These figures of 67.7 per cent and 52.4 per cent represent the general five year survival rate for patients with and without nodal involvement.

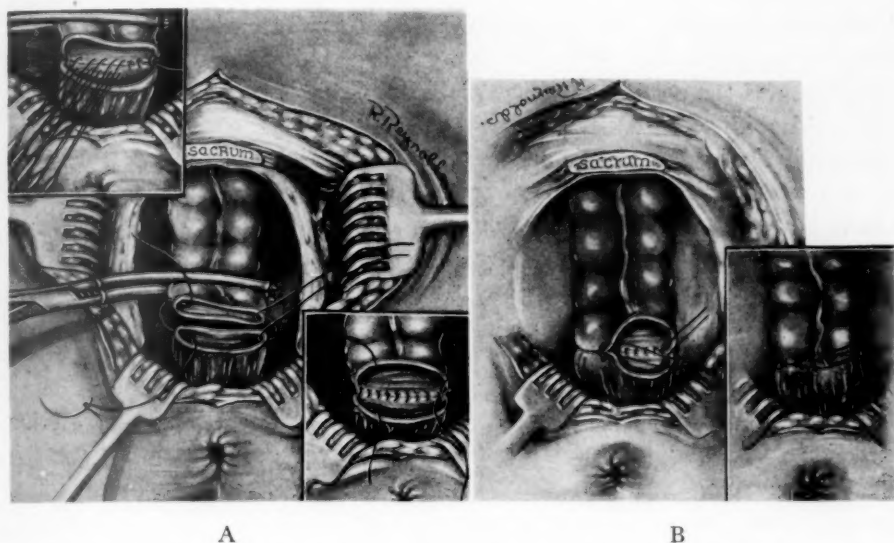


FIG. 7.—Anterior dissection with posterior resection and anastomosis. (A.) Traction sutures of catgut are placed at both angles of the anastomosis in such a manner that knots will be on the mucosal wall. A layer of interrupted catgut sutures is inserted on the anterior wall with knots on the mucosal side, inverting the margin of anastomosis. All of these sutures are inserted before any of them are tied. (B.) Several similar sutures, with knots on mucosal side, are inserted on the posterior wall. The anastomosis is completed by inserting a layer of figure of eight silk sutures on the posterior wall, lateral walls, and insofar as possible on the anterior wall. The incision is closed and a penrose drain is placed in the hollow of the sacrum and brought out at upper angle of incision.

It is also difficult for us to understand, after a detailed study of the anatomy of the lymphatics and the relation of these lymphatics and the levator ani structures to the rectal wall. However, if our analysis of these reports is correct, and granting unavoidable percentage error either way, the figures are significant and encouraging to those of us who believe in sphincter preserving operations in selected cases. Bacon,² with the modified Hochenegg or pull through operation, reports a 52.6 per cent incidence of five year cures. The accepted five year survival rate is probably between 50 and 60 per cent.

Some aspects of the technic are depicted in the accompanying illustrations and in previous reports.³⁻⁵ Improvements in technic have been made and

complications have gradually decreased. Drainage as a result of leakage at the site of anastomosis has occurred in about 50 per cent of the cases but in only one case did it persist for more than a few weeks. This followed Operation III and the patient died about six months after operation from recurrent carcinoma. We have almost routinely established a cecostomy as a decompressive measure. It is certainly more comfortable for the patient than nasogastric or nasointestinal suction, and is much more efficient when leakage occurs at the suture line. Also, we almost routinely drain the hollow of the sacrum by bringing a small drain out alongside the coccyx or sacrum.

It is our opinion that rectosigmoidectomy with anastomosis is a more satisfactory procedure than the pull-through operation. In our limited experience and observation with the pull-through operation, sphincter control has not been adequate, and the posterior leakage or incontinence is far worse than a colostomy. Also, it is our impression that the technic does not enable one to remove adequately the levator muscle and fascia and the adjacent lymphatics. In fact, we are now of the opinion that our Operation I—rectosigmoidectomy with anastomosis by abdominal dissection, resection and anastomosis—should not be used when the lower margin of the lesion is less than 10 cm. from the external anal margin. Of course lower anastomoses are possible and we have done them within 5 cm. of the anal margin, but at present we are doubtful of their feasibility. When the lesion is at or below the 10 cm. level, or when we believe it is adjacent to the levator ani structures, we advocate Operation II—rectosigmoidectomy with anastomosis by abdominal dissection with posterior resection and anal anastomosis—as this procedure enables one to remove the levator ani and adjacent structures.

SUMMARY

1. Sphincter preserving operations for carcinoma of the rectum merit further study and re-evaluation.
2. The recurrence of carcinoma of the rectum is dependent upon, and the result of, all modes of spread of carcinoma, *i.e.*, by direct extension, by venous channels, by lymphatic channels, and by transplant. All these factors have been discussed and more emphasis should be placed upon all of them.
3. In a collected series of 607 cases, only 5 patients (.8 per cent) had lymph node involvement more than 2 cm. below the lower margin of the tumor, yet it is estimated that 200, or approximately $33\frac{1}{3}$ per cent, of these patients died from recurrent carcinoma. Some factors other than node involvement below the tumor margin must be considered.
4. After experimental studies by injecting dye into the lymphatics of the perianal, anal and rectal regions, a practical classification of these lymphatics was made. This classification and the relationship between these lymphatics and the levator ani muscles and rectal wall have been discussed.
5. Patients with lesions below the 10 cm. level do not have as good a survival rate following radical abdominal-perineal excision as patients with lesions at a higher level. Wider excision of structures laterally to include the

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levator ani muscles, fascia and lymphatics is emphasized, when the carcinoma is located in the region of attachment, or adjacent to the levator ani structures.

6. Three sphincter preserving operations are presented for malignancy of the rectosigmoid and rectum. *Operation I*—abdominal dissection, resection and anastomosis; *Operation II*—abdominal dissection, posterior resection and anastomosis; *Operation III*—posterior dissection, resection and anastomosis.

7. *Operation II*—abdominal dissection, posterior resection and anastomosis—is recommended for all lesions below the 10 cm. level, as it permits radical excision of the levator structures.

8. For lesions involving the perianal skin and not the true anal canal, radium treatment, with or without radiation or dissection of the inguinal lymphatics, would seem to suffice from our studies. Malignant lesions within the anal canal should be extirpated by the radical abdomino-perineal resection.

9. The final conclusions on recurrence cannot be reached until a relatively large group of surgeons report on a sufficient number of cases, but the few reports being made on the five year survival rates are encouraging.

10. In patients who have had sphincter preserving operations, there is a better opportunity to examine and detect recurrence of cancer in the pelvis. Abdomino-perineal resection can then be done and the patient given another opportunity to survive the disease.

11. In our recent series of 51 consecutive cases of rectal carcinoma, there was an operability rate of 86.2 per cent and a resectability rate of 74.5 per cent. In patients with resectable lesions, a sphincter preserving operation was accomplished in 76.3 per cent and the abdomino-perineal resection with sacrifice of the sphincter mechanism was done in 23.6 per cent.

12. The operation should be fitted to the location and level of the disease rather than the surgeon fitting the disease to his choice of operation.

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DISCUSSION.—DR. VERNON C. DAVID, Chicago: There has been an increasing number of suggestions made for local operations of low-lying carcinoma of the rectum and for preserving the sphincters. All efforts to improve on the surgical treatment of cancer in the rectum, of course, are highly commendable, providing the patient's chances for long-term survival are not jeopardized.

At the present time our own figures show that long-term survival in low-lying cancer of the rectum is greatly lessened by more frequent local recurrences than in the group within the peritoneal cavity. This is true in spite of the most radical operations we have been capable of carrying out.

What are some of the reasons for this? Below the peritoneal reflection the rectum is enclosed by fascia and muscle attachments which bring the bowel in close continuity to the base of the bladder and soft parts, vagina, prostate, posterior urethra and so on.

Widespread resections of these structures are not feasible, and while portions of these structures are not infrequently removed (almost 20 per cent of our own patients had some portion of these organs removed), the tumor very frequently penetrates the bowel wall, and it is obvious that danger of local recurrence exists.

In addition, new patterns of lymphatic spread are present, some of which are not removable. This is true particularly of the vagina and levator muscles. It is undoubtedly true that it is difficult to inject some of the lymphatic pathways traversing the levator muscles, but it has been our experience that they exist. I have at present in the hospital a patient whose carcinoma of the rectum had definite lymphatic node involvement in the levator muscles at least three inches away from the tumor.

In my judgment this adds up to the necessity of performing the most widespread removal of soft parts possible in lowlying carcinoma of the rectum. The technical ability to do an end-to-end anastomosis deep in the pelvis or preservation of the continuity of the bowel, no matter how desirable, should always be considered secondary to permanency of cure of the patient.

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It also seems to me that advocacy of limited operation for cancer of the rectum should be accompanied, in the last analysis, by a declaration of the resectability rate, which is a very important thing, the mortality rate, the five-year-plus cure of the patient, the estimation of the malignancy of the tumor based on Broder's, Dukes' and our own criterion of lymph node involvement, and the definite statement as to whether the patients were a selected group or comprised unselected material.

It is only by some such standardization that we believe the truth which we all so earnestly seek shall be known.

DR. THOMAS E. JONES, Cleveland, Ohio: Dr. Best's experiments were on animals. Mine have been on humans. I have a report to make today on ten-year survival rates which might be of interest.

(Slide) In 1938 and 1939 we did 102 abdominoperineal resections for carcinoma of the rectum. Each specimen was subjected to minute pathological examination after the method of Drs. Dukes, Collier, David and Gilchrist with which you are all familiar.

We have a complete follow-up on 96 cases as demonstrated in these slides. Since they were completed we have a follow-up on three more cases so we know exactly what has happened to 99 per cent of this series. The figures referred to later include everybody as having died from cancer. Four cases with liver involvement at the time of operation were not excluded.

(Slide) This is an important slide. For purposes of information we arbitrarily divided the group into cases that had 0 to 5 nodes involved and those who had more than five nodes involved and you can see the difference in the survival rate. There were 78 cases with less than five nodes involved. At the end of five years, 44 out of 73 were alive—60 per cent. At the end of ten years, 14 out of 28, or 50 per cent were alive.

(Slide) However, in the cases that had more than five nodes involved (24 cases in this group), you will notice a marked difference. In 22 cases only five are alive, or 22 per cent. Twenty per cent were alive at the end of nine years and 11 per cent at the end of ten years. You will see then a tremendous drop from 60 per cent in the first group to 20 per cent in the second group. This is, of course, a plea for earlier diagnosis.

Now, let us look at a group in which there was venous involvement. In this group venous involvement was demonstrated in 10 per cent of the cases. However, if more meticulous examination were made with special stains, I feel that probably 20 or 25 per cent would show venous involvement.

(Slide) In the 92 cases without venous involvement, the percentage of survival parallels the group with less than five nodes involved—viz., 60 per cent 5-year and 50 per cent 10-year survivals.

(Slide) However, with venous invasion you will again notice a distinct drop. There were ten cases in this group. Three were alive at the end of five years, or 30 per cent, as against 60 per cent in cases without venous involvement. The 30 per cent survival rate in this group remained the same for the ten-year period.

(Slide) This final slide shows the over-all statistics:

Number of Cases: 102			
	Followed	Alive	Per Cent Surviving
5 years	97	51	52.5
8 years	94	46	48.9
9 years	73	36	49.3
10 years	32	14	43.7

I show these slides merely to point out that if these are the best results we can obtain with the most extensive operation, I do not see much use in fiddling around with smaller or so-called sphincter-saving procedures.

DR. CLAUDE F. DIXON, Rochester, Minn.: My remarks will be limited to the treatment of cancerous lesions which occur in the lower half of the rectum.

First, I think that we are in agreement that the results which follow the surgical removal of cancerous lesions affecting the colon and the rectum are less satisfactory when the lesions occur in the most distal segments of the large intestine.

It is understandable why some of us have been eager to attempt to maintain the sphincter and normal bowel control on removal of the lower part of the rectum by means of the method of Hochenegg. A small pedunculated or sessile carcinoma of the lower portion of the rectum doubtless may occasionally be cured by a surgical procedure other than radical resection with establishment of some type of abnormal or artificial anus. The fact remains, however, that the majority of cancerous lesions of the lower half of the rectum are not small lesions and they spread centrifugally as well as proximally by means of the lymph and blood stream and by direct extension.

For several years I have been of the opinion that the surgical removal of cancerous lesions, situated low in the rectum, requires an even more radical operation than the Miles procedure, for involved lymph nodes may be found in the pelvic fascia and levator ani muscles at a distance of 2 to 3 inches (5 to 7.5 cm.) from the lesion in the bowel. For this reason, in a large series of patients suffering from cancer in the lower part of the rectum, I have carried out a two-stage combined abdominoperineal resection. The abdomen is explored through a low left rectus incision. If the abdomen is found to be free of metastatic processes, the bowel is divided in the distal portion of the descending colon and the proximal end is brought out through the abdominal wall in the left lower quadrant by means of a stab wound, muscle-splitting type of incision.

Next the posterior parietal peritoneum is opened, the superior hemorrhoidal vessels are ligated and severed, and then the first portion of the sigmoid colon with its mesentery is removed. The bowel is now divided in the region of the midsigmoid, the proximal end of the remaining segment is inverted and allowed to remain free in the upper portion of the pelvis, the small defect or the incised posterior parietal peritoneum is repaired, and the abdomen is closed in the usual manner. Later (in ten to 12 days) a radical perineal operation is carried out, at which time portions of the gluteal muscles, the levator muscles and pelvic fascia are removed. The peritoneum is opened and the rectum and remaining segment of sigmoid and mesosigmoid are removed. Then the peritoneum is closed, and the wound is packed with four yards (about 366 cm.) of gauze four inches wide (10 cm.) which is removed on the fourth postoperative day. This procedure is carried out with the patient in the reverse Trendelenberg position and is, I believe, radical in the region of the growth which to me seems to be indicated.

My personal experience with the pull-through operation is that it frequently fails because of local recurrence of the lesion or because the mechanism of the involuntary sphincter (internal sphincter) is destroyed. Finally, I think it well to keep in mind that the meticulous work of David and Gilchrist, and of Collier and his associates has demonstrated that, in cases of rectal cancer, involved lymph nodes may easily be overlooked. Therefore, as a rule, I think that some type of radical operation is the operation of choice in the surgical management of cancer of the lower portion of the rectum.

DR. R. KENNEDY GILCHRIST, Evanston, Ill.: Gentlemen, I think one of the troubles here is what the different surgeons mean by a "radical" operation; secondly, where is this cancer that they are discussing?

It is very interesting to go through the pathological material removed by men who are trained under pretty much the same auspices in one single institution, and to see the different amount of tissue and the lymph drainage removed by various surgeons,

SPHINCTER PRESERVING

and then go back and look at your own specimens; you will be surprised. I find, too, that I have been much less radical some times than other times.

What is a radical operation for cancer? The word is used by almost every surgeon who operates for cancer. To my mind it means the removal of the tumor, the surrounding soft parts as widely as they can be removed, and all of the primary and all of the first alternate group of lymph nodes that drain the area, if it is possible to do so, and still have a living patient who can carry on his normal life.

The studies on lymphatic drainage shown here confirm what has been shown before. Squamous cell carcinomas that arise in the skin and involve the mucosa of the bowel, or come up behind the mucosa, we have demonstrated to have lymph node metastases upward along the superior hemorrhoidal drainage as well as to the inguinal nodes. Of course that is just what one would expect from an anatomical study of the lymphatics.

By the same token, those adenocarcinomas which arise in the mucosa and have extended downward to involve the skin—we have seen some where there has been lymphatic involvement of the inguinal nodes as well as to nodes along the superior hemorrhoidal vessels. Any local operation for cancer at this level must be viewed with a good deal of reserve. Certainly it cannot be called radical surgery if you do not take out the regional lymph nodes.

(Slide) This is not new. This man had a very lowlying carcinoma.

(Slide) Rouviere showed this same thing, that there are lymph channels very low in the rectum which may go directly to the nodes at the promontory of the sacrum. This patient had a lesion just above the mucocutaneous line, and yet there are involved lymph nodes at or above the promontory of the sacrum, and of course no posterior resection is going to remove these.

To my mind the superior hemorrhoidal arteries should be removed at least an inch and a half, and preferably two inches above the promontory of the sacrum if you have any hope of removing the primary set of filters to the lower bowel. The lateral spread has been well discussed.

I would urge upon you two other things. Let's have a common landmark that we can identify. I know of a patient in Chicago who had a proctoscopic examination by a medical man. He found a tumor about nine or ten centimeters above the mucocutaneous line. The patient did not want a colostomy; she went elsewhere and had a transverse colon resection for a carcinoma which had intussuscepted all the way down. If we are to use centimeters on the proctoscope as a landmark, this tumor would be classified as one at nine centimeters.

The landmark you can see any time on the specimen or in the belly, and that needs no ifs, ands or maybes, is the deepest part of the pelvic peritoneum. Of course, as Dr. David has pointed out, this region has an anatomical importance as far as lymphatic drainage and fixation to the contiguous structures which may set up new lymphatic drainage patterns. The anterior peritoneal reflection is the landmark that I would urge, rather than centimeters, because it is reproducible and needs no further identification. For many years we have often re-established continuity where lesions were ten or 12 cm. on the proctoscope by obstruction resection. I was brought up on that.

If you remove the bowel and its mesentery an inch and a half or two inches below the tumor, and if the tumor is covered completely by peritoneum on the anterior surface and if there is no marked enlargement of the lymph nodes or fixation to other structures, there is no reason why you should not attempt to re-establish continuity, but if any of these unfavorable features are present, then you must do the most radical thing, namely, an abdominoperineal resection.

DR. R. RUSSELL BEST, Omaha, Neb.: I would like to thank the discussers for their interesting and informative remarks.

First, I would like to make a few remarks about the pull-through operation. The operations I have seen done, and also those depicted in the literature, do not seem

radical enough in the region of the levator ani muscle. In this whole picture we have three avenues of spread. I plead that we stay just as high above the lesion as possible, because that is the most direct method of spread. From our studies, I also plead for more and wider dissection of tissues in the region of the levator ani muscles. When it comes to considering the area below the lesion, our investigations lead us to believe that the sphincter mechanism can be saved more frequently than it has been in the past.

Theory and emotion must be replaced by experience in sphincter preserving operations and a final tabulation of the end results. Personally, I do not believe that sufficient experience has been had by a sufficient number of surgeons in a sufficient number of cases over a long enough period of time to unequivocally make a statement. In this presentation, I have merely attempted to evaluate the sphincter preserving procedures based upon existing pathologic-anatomical knowledge, some experimental studies and a limited experience.

In the pull-through procedure, I do not believe we have good control in many cases and if we do not have good control, whether by anastomotic procedure or pull-through, I believe it is better to have an abdominal anus. A well and tried fecal discharging stoma on the abdominal wall is far better than a hidden irritating fistulous opening in the perineum.

Next, a few remarks on technic should be mentioned as related to this group of patients.

(Slide) In our cases we have always established a cecostomy and have always drained the pre-sacral space by a small incision along the coccyx in all operations where the anastomosis is below the peritoneal reflection. In other words, in Operations I, II and III these two technical maneuvers seem indicated by us to lessen morbidity and mortality.

(Slide) In our posterior approach in Operation II, we go more widely than depicted in these drawings. From our experimental studies, we are now more conscious about wider excision in the region of the levator ani muscle in the abdomino-perineal operation and in the sphincter preserving procedures.

(Slide) This shows the completion of the anastomosis and placing of a drain in the hollow of the sacrum, because in about 50 per cent of our cases (I am reluctant to say it), we have had some fecal drainage although in only one case has it been prolonged over any number of weeks.

EXTENSION OF CARCINOMA OF THE STOMACH INTO THE DUODENUM AND ESOPHAGUS*

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THERE IS CONSIDERABLE REASON to believe that many surgeons today are performing inadequate removal of cancer of the stomach, because of deficient knowledge as to the nature of its spread. The poor results which are generally recognized to exist so far as complete cure of this disease is concerned are usually ascribed to the fact that in the vast majority of cases the cancer is far advanced by the time operation is performed and dissemination to distant areas has already occurred. On the other hand in some of the large bulky lesions the tumor remains localized in the stomach for a considerable time without metastases. While many efforts to improve the situation as regards earlier diagnosis are being made, it seems unlikely that any major improvement will occur in the near future. For that reason it seems desirable that surgeons should review their present methods, and in the light of present knowledge of the spread of the disease, see if changes in them can lead to increase in the percentage of cures.

For the past 18 months we have been engaged in a study of the extension of cancer of the stomach into the wall of the organ itself and also into the duodenum distally and the esophagus proximally, using large microscopic sections. This investigation has been supported in large part by a research grant from the National Cancer Institute, U. S. Public Health Service. Previous studies of such extension have been made, but though a number of reports concerning it have been recorded they have not received wide publicity, and we are convinced that many surgeons who are resecting stomachs for cancer are unaware of the importance of the local extension which frequently occurs.

In 1934, Verbrugghen¹ reported a study of 50 cases of cancer of the stomach with regard to the local extension of cancer in the gastric wall. His material consisted of specimens removed surgically at the Mayo Clinic. He found that the degree of extension varied considerably, depending largely on the degree of differentiation of the tumor microscopically. In many infiltrative types the extension was found to be considerable and unpredictable. On the other hand, in those lesions which were well localized grossly, there was found to be microscopic extension as much as 35 mm. from the apparent edge of the tumor. Verbrugghen therefore recommended that a margin of at least 4 cm. of apparently normal tissue be removed beyond the edge of well circumscribed lesions,

* Supported in large part by a grant from the National Cancer Institute, U. S. Public Health Service. Read before the American Surgical Association, St. Louis, Mo., April 21, 1949.

and stated that even wider margins were desirable in lesions less well defined.

In 1936, Castleman,² in a review of 134 surgical and 65 autopsy specimens of the stomach, by careful microscopic study, found infiltration of cancer cells beyond the pylorus into the duodenum in 21 cases, or 10.5 per cent. That such spread could occur was not generally recognized or mentioned in textbooks. As a matter of fact, it has been a popular misconception that cancer of the pyloric end of the stomach remains well confined within the stomach itself and does not spread beyond the pylorus. He reported that the extent of penetration of the duodenum varied from 4 to 23 mm. and he therefore recommended that at least 3 cm. of duodenum be removed in resecting every carcinoma of the pyloric end of the stomach.

In 1941, Collier, Kay, and McIntyre³ published their very important contribution to our knowledge of the lymphatic spread of cancer of the stomach, especially in the extramural lymphatic system. In the 53 cases studied by them, principally with regard to the lymphatic spread, they mention that in 14 or 26.4 per cent there was microscopic evidence of extension of the cancer into the duodenum.

Pack and McNeer⁴ in a recent article have pointed out the frequency with which cancer of the cardiac end of the stomach has invaded the wall of the esophagus. This involvement, just as in the duodenum, is likely to be only microscopic, and therefore imperceptible to the surgeon on gross palpation, and may extend for considerable distances. They state that this extension has been observed so frequently, and may extend so far, that their routine procedure is to make a frozen section of the transected esophagus, and anastomosis is not done until such examination has been reported negative for cancer.

The material for our study has been obtained principally from the operating rooms of the Cincinnati General Hospital and the Christian R. Holmes Hospital. Both of these hospitals are under the professional direction of the College of Medicine of the University of Cincinnati, and the operations were performed by members of the faculty of the Medical College and the resident house staff. In addition, a number of specimens were obtained from four private hospitals in Cincinnati, so that many surgeons participated in furnishing the material, and examination gives a picture of how resections of the stomach are performed in the city as a whole. A number of autopsy specimens have been studied during the same period and by the same method. These are not being reviewed at this time, as they may be considered by some as representing more advanced stages of the disease than those which were considered operable and removed surgically.

The steps involved in the study of our cases included the following. The pathologist received the specimen as promptly as possible after its removal. Usually he was in the operating room to get it immediately. The specimen was opened and after gross examination and description, was photographed in color and black and white, pinned out on a cardboard or thin board to minimize shrinkage, and fixed in formalin. After fixation the artist made a sketch of the lesion, and the portion taken for microscopic study was indicated on this sketch

by dotted lines. Large blocks were taken through the entire lesion and through the adjoining stomach and duodenum or esophagus to the edge of the specimen. In a number of instances one block sufficed to reach from one end of the entire specimen to the other; sometimes two or more were necessary. The chief limitation to the size of the block was the size of the slide and cover slip, the dimensions of which are approximately 3 by 5 inches. The tissue was imbedded in paraffin, cut on a special microtome, usually at 10 micra thickness, and stained with hematoxylin and eosin. The thinness and general excellence of the sections was such that careful microscopic study was possible. In general the blocks were 5 to 10 mm. in thickness, and though serial sections were not made, a number of sections were prepared from several levels in each block so as to give a better picture of the extent of invasion.

The total number of operative specimens examined to date is 47 divided as follows:

TABLE I

Partial gastrectomy, including duodenum.....	34
Partial gastrectomy, including esophagus.....	6
Partial gastrectomy, including no duodenum or esophagus.....	5
Total gastrectomy.....	2
Total.....	47

In most of the tumors of the distal half of the stomach, the resection was carried beyond the pylorus. In a few, although the gross description and photograph seemed to indicate that some duodenum had been resected, no duodenal mucosa could be recognized microscopically. Of the total of 36 cases showing duodenal mucosa microscopically, nine or 25 per cent showed invasion of the duodenum by carcinoma. In six of the 36 cases the lesion was in the body of the stomach and grossly more than 5 cm. from the pylorus. If these are excluded and only the 30 cases considered in which the lesion was located in the antrum and within 5 cm. of the pylorus, the percentage of cases in which duodenal invasion was found is 30 per cent, or 9 cases out of 30. The length of extension could not be measured too accurately, but varied considerably, being only 3 mm. in two cases, from 7 to 15 mm. in four cases, 20 mm. in two cases and 60 mm. in one case. These measurements were made directly on the large sections, and do not allow for any shrinkage which had occurred. (See Table II.) The invasion into the duodenum seemed principally to be by direct infiltration of the muscle or extension in the subserosal lymphatics. In only three cases was it in the submucosa, one of the chief sites for extension in the stomach and esophagus. In a number of cases an isolated lymph node adjacent to the duodenum beyond the pylorus displayed metastasis without any actual cancer being found in the duodenal wall itself. Such instances have not been listed as showing extension into the duodenum, though it is obvious that removal of a node in this location *en bloc* with the rest of the specimen would require resection of the duodenum. In practically all cases there was no gross

evidence of invasion of the duodenum, and it was recognized only microscopically.

The greatest extension encountered was 60 mm. as measured on the resected specimen. In this case, however, carcinomatous infiltration was

TABLE II.—*Degree and Location of Extension into Duodenum*

Case No.	Extent	Location
11.....	3 mm.	Mucosa
12.....	60 mm.	Muscle and subserosa
21.....	15 mm.	Muscle
23.....	7 mm.	Muscle
59.....	20 mm.	Lymph node and muscle
65.....	12 mm.	Subserosa
78.....	10 mm.	Submucosa
79.....	3 mm.	Mucosa and muscle
80.....	20 mm.	Muscle

present at the line of division of the duodenum so that it obviously extended farther than that. This patient was operated upon by one of us (MMZ), and at the operating table peculiar radiating lines were seen extending in the subserosa of the duodenum well into the second portion. It was suspected that this might represent carcinomatous extension, but was unlike any seen previously and therefore not regarded as characteristic. The patient had a deep ulcer, but there was free hydrochloric acid in the gastric secretion, and there was some question whether the patient had cancer or a benign ulcer. Radiating lines similar to those seen in the serosa of the duodenum were found extending over the pancreas and the retroperitoneal tissues from near the base of the ulcer. No enlarged lymph nodes nor metastases in the liver could be made out. During resection more duodenum was removed than usual in order to get a good specimen of the unusual appearing tissue, though the total visible extent of what later proved to be cancer could only have been removed by total pancreatectomy and duodenectomy. The microscopic picture shows extensive cancerous infiltration in the subserosa and muscularis up to the line of resection. As can be seen in Fig. 1, the section resembles a typical benign gastric ulcer, which is just the way it appeared at the operating table. There is, however, both scirrhus and mucoid carcinoma present in the base and wall of the ulcer with wide spread extensions both in the muscle and in the subserosal lymphatics. Most of these groups of cancer cells are too small to be seen in Fig. 1. On low power examination, Fig. 2, they can be seen to extend, as has already been noted, to the line of transection of the duodenum, certainly several inches from the distal edge of the ulcer. Proximally, they extend in the subserosa to arrow No. 3, Fig. 1, 40 mm. from the proximal edge of the ulcer. The patient developed jaundice about four months after operation. Shortly thereafter the liver enlarged rapidly and death occurred within six months.

There were six cases of cancer of the cardiac end of the stomach, all removed with some attached esophagus. All but one of these showed microscopic invasion of the esophagus, although this was evident grossly in only two cases. Microscopic extension into the esophagus occurred principally in

EXTENSION OF CARCINOMA OF STOMACH

the submucosa with additional extension in the longitudinal and circular muscle in some cases. It consisted usually of small isolated clumps of cancer cells, apparently lying within lymphatic channels. It is our impression that the extension developed first in the submucosal lymphatics and as it progressed, extended outwards into the lymphatics in the muscle layers. The longest extension measured was approximately 25 mm., but at that point the esophagus had been resected, and it is impossible to say how much farther extension had

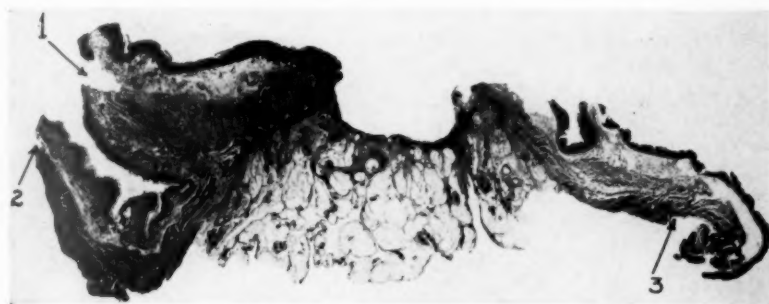


FIG. 1.—Section of cancer of stomach resembling benign ulcer. (1) Junction of gastric and duodenal mucosa. (2) Cancer cells in serosa and muscularis to edge of transection 60 mm. from pylorus. (3) Cancer cells in serosa 40 mm. from the proximal edge of the ulcer.

occurred. This is illustrated in Figs. 3, 4, and 5. The tumor itself, as can be seen in Fig. 3, is a small, sessile adenocarcinoma with superficial ulceration. It measured only about 35 mm. in diameter and seemed to be rather sharply localized. The exact junction of the gastric and esophageal mucosa cannot be recognized but is presumably at about the level of arrow No. 1 in Fig. 3. Distally in the stomach small clumps of cancer cells can be seen in the submucosa as far as arrow No. 2, Fig. 3, approximately 45 mm. from the edge of the tumor. These are shown in a low power photomicrograph in Fig. 4. In the muscularis they do not extend quite so far, about 35 mm. from the edge of the tumor. Proximally, the tumor cells extend both in the submucosa and in the muscularis to the line of transection of the esophagus,



FIG. 2.—Low power photomicrograph. (x 20 before reduction) of area 2 in Fig. 1. Arrows point to cancer invading muscularis and serosa to edge of transection.

about 25 to 28 mm. from the upper end of the tumor. This part of the section is shown in low power magnification in Fig. 5.

The extensions in the wall of the stomach varied within wide limits and were unpredictable. In many of our cases the microscopic spread was not

FIG. 3

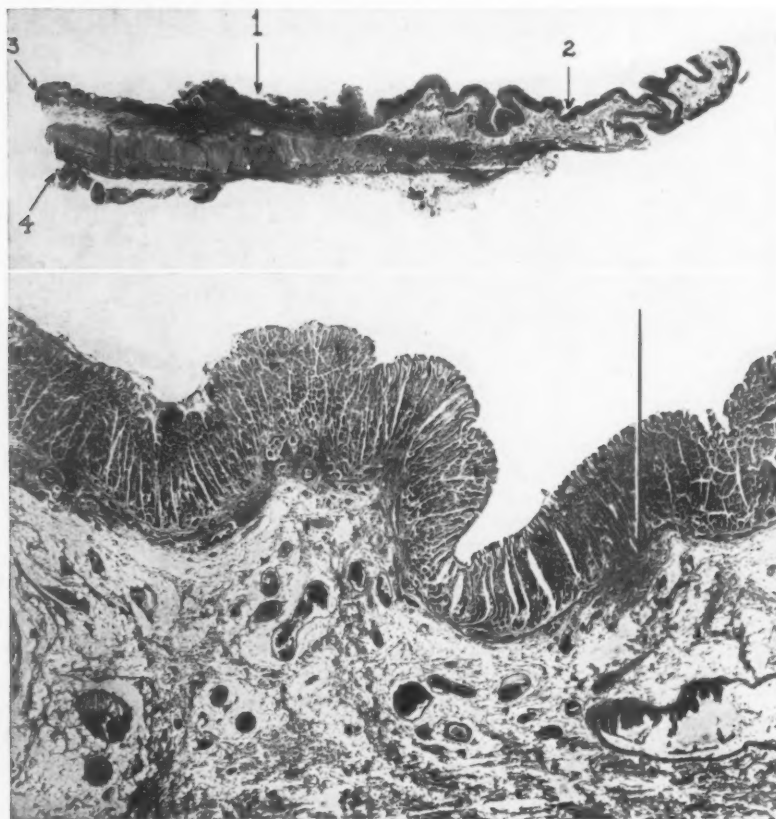


FIG. 4

FIG. 3.—Section of cancer of cardiac end of stomach including stomach and esophagus. (1) Approximate position of gastro-esophageal junction. (2) Limit of extension of cancer into stomach in submucosa. (3) and (4) Extension of cancer in submucosa and muscularis to point of transection of esophagus.

FIG. 4.—Low power photomicrograph ($\times 20$ before reduction) of area 2 in Fig. 3. Arrow points to limit of cancer extension in submucosa. Tiny clumps of cancer cells can be seen in the submucosa almost continuously from here to the tumor.

significantly beyond the obvious gross limits of the tumor. In most instances it varied from 5 to 10 mm. but in some cases was as much as 15 to 25 mm. We were unable to find any correlation between the microscopic nature of the tumor and the extent of microscopic spread. Neither was there any way in which we could predict from the gross appearance how far extension would occur. In

general it seemed that the ulcerative lesions which grossly resembled benign ulcer were likely to spread most widely beyond the gross limits. In the stomach as in the esophagus, the principal site for extension seemed to be in the submucosal lymphatics. In scirrhous carcinomas, however, direct extension in the muscle was likely to be present, though this was usually evident grossly or at least suspected because of thickening and induration. The submucosal extensions as a rule were not associated with thickening of the wall or palpatory evidence, and consisted of inconspicuous clumps of cancer cells as seen in Fig. 4.

It was noted in Table I that in five cases no duodenum or esophagus was present in the sections. These represented either small lesions located in the fundus, or else cases in which the distal end was transected so close to the pylorus that all of the duodenum removed was crushed by the distal clamp. One of these was a very small, and presumably early, lesion which is of considerable interest. In this patient, gastro-intestinal roentgenological study for discomfort due presumably to spastic colitis demonstrated a polyp in the fundus of the stomach. Gastroscopic examination confirmed the presence of the polyp, but malignancy could neither be diagnosed nor excluded. At operation within ten days of the discovery of the lesion we also were in doubt as to the nature of the polyp, which was soft and about 2 cm. in diameter. A radical resection nevertheless was performed and the microscopic section showed a benign polyp about $1\frac{1}{2}$ by 2 cm. on a short pedicle. Just at the base of the polyp was a small carcinoma about 12 by 5 mm. in diameter. Even this small lesion showed one tiny nest of cancer cells in the muscularis about 3 mm. from the edge of the tumor. No involvement of any lymph nodes was found. Only a small segment of duodenum was removed at operation since the tumor was at least 4 inches from the pylorus. No duodenal mucosa was seen in the section, which undoubtedly was due to the fact that it was crushed in the distal clamp.

The two total gastrectomies in this series were for extensive lesions, one for a large carcinoma of the lesser curvature, and the other for a case in which there were multiple malignant polyps. In neither instance could the

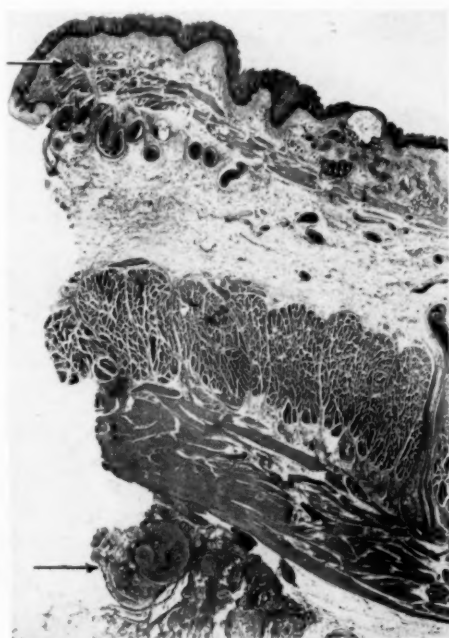


FIG. 5.—Low power photomicrograph ($\times 12$ before reduction) of areas 3, 4 in Fig. 3. Arrows point to tiny clumps of cancer cells in submucosa and muscularis.

surgeon be sure about the exact extent of the lesion, and therefore performed total gastrectomy in order to keep well beyond any extensions of the tumor. In neither case was there invasion of either duodenum or esophagus, grossly or microscopically.

From an examination of the microscopic sections, a significant number of the cases showed that the surgeon had either cut through cancer at one or the other end of the specimen or had resected so close to tumor as to make one believe that there was insufficient margin of normal tissue. In actual figures this is shown as follows: Total cases 47. Cancer in transection line of stomach seven, of duodenum one, of esophagus one. Thus there were nine instances in the 47 cases in which the surgeon cut across carcinomatous tissue in the resection, approximately 19 per cent of the cases. It is interesting to note that

FIG. 6

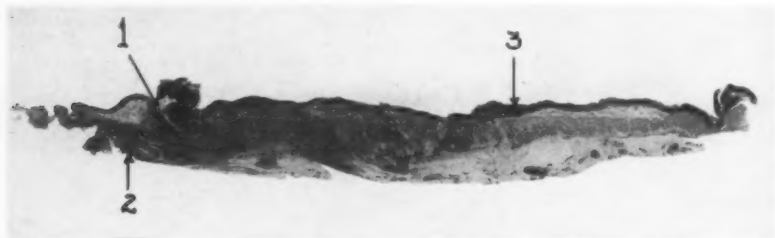


FIG. 7

FIG. 6.—Section of ulcerative cancer of prepyloric area. (1) Junction of gastric and duodenal mucosa. (2) Extension of cancer into muscularis of duodenum. (3) Proximal extent of cancer in submucosa of stomach.

FIG. 7.—Section of ulcerative cancer of prepyloric area. (1) Junction of gastric and esophageal mucosa. (2) Distal extent of cancer microscopically. (3) Proximal extension of cancer in muscularis and serosa to line of transection.

in 1941 Coller and his associates in the article previously cited made somewhat similar observations. It must be emphasized that just as in Coller's series a fair number of these patients presented far advanced lesions, and many of the resections were palliative procedures and were not considered by the surgeon as being curative. Several such cases were done by one of us (MMZ), and resection was performed, even though it was obvious that not all of the carcinoma could be removed, in an effort to relieve nausea, anorexia, pain, obstruction, bleeding or vomiting, and with the expectation that death would

occur from metastases or general debility before local recurrence led to the return of symptoms referable to the stomach itself.

Consideration of the data presented here, together with that presented by others, leads us to believe that many surgeons not only are not being sufficiently radical as regards removal of the extramural lymphatics, but that also they do not remove sufficient amounts of stomach, of duodenum, or of esophagus. In all carcinomas of the distal half of the stomach, in addition to removal of the great omentum, and as much of the gastro-hepatic ligament as is possible, the first portion of the duodenum should also be removed. Just how far the resection should be carried proximally in the stomach cannot be stated in centimeters or inches, but it would seem wise to suggest that the surgeon decide what he regards as a safe margin proximal to the tumor and then actually resect an inch or two more. Naturally the question arises as to the desirability of routine total gastrectomy in the treatment of gastric cancer. This has already been suggested by Longmire.⁵ Our own experience with total gastrectomy leads us to believe that marked feeding difficulties occur in a fairly large proportion of patients, though others seem to have little or no difficulty in eating after apparently identical procedures. On account of these feeding difficulties we are not willing as yet to recommend routine total gastrectomy.

For cancers of the cardiac end of the stomach we believe that resection of some esophagus along with the cardiac end of the stomach is necessary. Just how much esophagus should be removed is not certain, but 1 to 1½ inches may prove to be too little. The plan recommended by Pack seems to be worth consideration by all of us, *i.e.*, frozen section of the cut end of the esophagus before anastomosis is done.

We have been more and more impressed by the value of a combined abdomino-thoracic incision for the removal of all cancers of the stomach, whether they be in the distal or proximal half of the organ, and whether a total gastrectomy is to be done. For this purpose we have been using the incision described by Carter⁶ for splenectomy. This incision gives adequate exposure of the duodenum so that its resection can be carried out readily. It gives admirable exposure of the gastro-hepatic ligament and permits easy access for removal of gland-bearing tissue along the lesser curvature of the stomach, and with slight modification allows exposure and removal of a considerable segment of the lower esophagus. We are now using it almost routinely in all cases of cancer of the stomach.

SUMMARY AND CONCLUSIONS

Forty-seven cases of cancer of the stomach have been studied with reference to extension of the tumor into the wall of the stomach and into the duodenum and esophagus.

In 30 cases in which the tumor lay grossly within 5 cm. of the pylorus, nine or 30 per cent showed carcinomatous invasion of the duodenum. The extent of this invasion varied from a few millimeters to several centimeters. In

practically every instance the invasion was only evident microscopically and was not recognized grossly.

In six cases of cancer of the cardiac end of the stomach, five showed invasion of the esophagus, though this was apparent grossly in only two of them. The greatest length of microscopic invasion beyond the apparent edge of the tumor was 25 mm.

In the wall of the stomach, microscopic invasion varied greatly with regard to its extent.

No correlation could be recognized between the gross or microscopic appearance of the tumor and the likelihood of invasion.

In view of these findings it seems advisable to reaffirm the need for wide local excision in resecting cancer of the stomach. In order to accomplish this easily, a combined abdomino-thoracic incision is recommended.

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DISCUSSION.—DR. ALEXANDER BRUNSCHWIG, New York City: I simply want to use Dr. Zinninger's excellent presentation to present a few photographs that might be of interest to the Association in connection with the subject of gastric cancer. These are photographs that relate to the initial operation that Billroth performed in 1881.

(Slide) This is the specimen of the first gastrectomy as it is preserved today in Vienna. You will note that Billroth did remove quite a generous part of the first segment of duodenum. The date of the operation was January 19, 1881. The photograph was sent to me by Professor Denk of Vienna, who was elected to honorary membership in this society last year.

(Slide) This is the front sheet of the original history of this epoch-making case. There is no signature to this discussion of the patient's symptoms. The physical findings begin about here. We don't know who wrote the history, although presumably it was one of Billroth's assistants.

(Slide) This is a postoperative note made the day after operation, and again it is unsigned. This is a freehand pencil sketch which is remarkably well preserved, with the pylorus indicated here, the tumor here, and the cuff of the duodenum here.

It is interesting to recall that Billroth was rather fearful of criticism, and scheduled this operation late one afternoon under the seats of his amphitheater, and only two or three of his assistants knew that he was going to do it. They were the only audience present.

(Slide) This is the final note. "Died of metastases after pylorotomy for cancer," and it is unsigned. The patient had lived four months.

THE END RESULTS OF COMPLETE VERSUS INTRACAPSULAR REMOVAL OF ACOUSTIC TUMORS*

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THE SO-CALLED ACOUSTIC TUMORS are the common type of intracranial new growths situated in the cerebellopontile angle. Although they are benign, encapsulated, non-invasive lesions, their removal in the early days of neurosurgery was attended with such a high mortality (75 to 85 per cent) as to be prohibitive, and even then it is doubtful whether complete removals with useful survival of the patients were ever accomplished.

In 1917, therefore, Harvey Cushing² introduced the method of what he termed the "intracapsular extirpation" of these tumors. This meant that after incising the capsule, the contents of the growth within were more or less completely taken out with a blunt curet combined with suction. In this way it was inevitable that some portions of the tumor would remain inside the capsule, as the latter was left *in situ*, and recurrence took place at varying intervals, many within two to five years following the operation, although a fair number of patients lived for much longer periods. However, the intracapsular operation constituted a great step forward, since, for the first time, it offered patients with acoustic tumors a good chance at least of coming through the operative procedure. The immediate mortality was reduced, at least in Cushing's hands, from prohibitive figures down to 20 per cent at first, and later to less than 10 per cent.

On the other hand, it became obvious that the intracapsular removal was far from ideal, both because of almost certain recurrence and because the five-year mortality after this procedure was exceedingly high—56 per cent in Cushing's series, from figures given by Eisenhardt⁷ in 1935. For this reason Dandy³ made a preliminary report in 1922 of an operation for the complete removal of acoustic tumors, followed in 1925⁴ by recording five such complete extirpations without mortality. In 1934⁵ he introduced an important technical advance in the unilateral approach through a relatively small bony opening instead of the wide bilateral exposure used hitherto.

Since these early articles there have been surprisingly few reports by neurosurgeons concerning the end results of operations for acoustic tumors by either of the methods mentioned. In 1934 Olivecrona¹⁰ reported 31 cases in which complete extirpation had been performed with a 19.4 per cent mortality. He stated that the end results and useful survival in this group were far better than in his previous series of intracapsular extirpations.

* Read before the American Surgical Association, St. Louis, Missouri, April 21, 1949.

In 1939 the present authors reported⁸ a series of 35 patients with acoustic tumors on whom they had operated during the previous seven years. Seven of those patients had intracapsular removals, and although the operative mortality was not great, all but one of these patients died subsequently. Nine other patients had one or more previous attempts at removal of their tumors elsewhere, and although we were eventually able to extirpate their growths completely they need not be considered in the present connection, since the difficulties and hazards in this group are exceedingly great. The remaining 19 patients had not been operated on previously and a complete removal of their tumors was accomplished. The operative mortality in this latter group was 10.5 per cent, and it was stated that, aside from the two postoperative deaths and four others who showed considerable disability, the remainder (68 per cent) "were able to get about perfectly well by themselves and, for the most part, to resume their former occupations."

In 1942 Nielsen⁹ made a careful study of Olivecrona's large series of 130 acoustic tumor patients operated on between the years 1930 and 1939. Twenty-eight of these patients had intracapsular extirpations of their tumors and Nielsen also gave mortality figures for 34 patients with this type of operation performed previously by Olivecrona, making a total of 62 intracapsular removals. There were likewise 75 patients who had had their tumors completely taken out. Without going into the details of Nielsen's statistics it was pointed out that the immediate operative mortality from intracapsular removal was between 27 and 28 per cent and that within five years the death of 16 more patients had occurred, making the total five year mortality for this group roughly 56 per cent. On the other hand, the operative mortality in the completely removed group was 18.7 per cent, and although four of these patients died subsequently, in only one was there the possibility that death was due to tumor recurrence.

In regard to useful survival, that is, either full or somewhat diminished earning capacity, Nielsen stated that 75 per cent of the patients having intracapsular extirpations came into this category. This figure refers obviously only to those patients who survived the operation and the subsequent five-year interval, since only 27 patients, or roughly 44 per cent of the original 62 in this group, survived. As will be shown later, we feel that the only real way of determining correct end results is to base the percentage of useful survival on the total number of patients operated upon. If such a comparison is made, the 75 per cent, or 21 of the 27 survivors, would represent 33.8 per cent of the total 62 patients with intracapsular removals who were leading useful lives.

In the group of complete extirpations Nielsen has again followed the same method of basing the percentage of patients living useful lives on the number surviving the operation and the five-year interval. His figure for this group by this method would be 80.4 per cent, but if one bases the percentage on the total number of patients operated upon, namely 75, it is found that roughly

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60 per cent of patients who had complete removal of their tumors were living useful lives at the time they were studied. As can be seen, this figure is nearly twice the percentage of those in the intracapsular group.

In 1943 Dandy* summarized his experiences with 46 patients who had complete removal of their acoustic tumors. There were five deaths in this series, an operative mortality of 10.87 per cent. In connection with the end results he stated that two patients died within one year after leaving the hospital. Concerning useful survival the following statement was made: "So far as I know all the remaining cases are living and well. With few exceptions all are active, and many of them are carrying on their former work in full capacity. Perhaps half a dozen have some degree of uncertainty in walking and have slight ataxia." It is impossible to get any useful numerical percentage as to satisfactory survival in this series, especially since the author includes "several" small tumors which "were encountered when operating for trigeminal neuralgia by the cerebellar route." These would not be considered as the usual type of relatively large tumors which most authors have dealt with in tabulating both their mortality as well as their end results. However, it is safe to assume that Dandy's figures would at least be as good as others who have made similar studies.

Olivecrona's last report in 1948¹¹ is concerned with 250 operations for acoustic tumors. Of these, 185 had complete extirpations, and in 34 the tumors were subtotally removed. In only 26 was the intracapsular method employed. The operative mortality for the entire group was 23.6 per cent, and for the 185 from whom the tumor was completely removed was 24.3 per cent. Ten of these latter died from one to 15 years after leaving the hospital. Because of the impossibility of anything like complete follow-up figures in Olivecrona's series (since many of his patients were in European countries during the war), only rough estimates of the percentage of patients living useful lives can be made. From his figures there were 118 patients having complete tumor removals who had full or somewhat diminished earning capacity. This would be 63.2 per cent of the original 185 patients operated upon by this method, but would represent 84.2 per cent of the 140 who survived the operation and left the hospital. Twenty-six of Olivecrona's patients had the intracapsular operation. Seven of these died postoperatively and seven others subsequently, thus making the eventual mortality 53.8 per cent. Of the remaining twelve, nine, or 75 per cent, were in useful life, but based on the original 26 patients this represents only 34.6 per cent.

To summarize the data as given by Olivecrona and by Nielsen from Olivecrona's clinic one may say that the five-year mortality for complete tumor removals (including the operative mortality) would be roughly 25 per cent, whereas with the intracapsular operation for a like period the mortality would

* Article was apparently not published. Manuscript was sent to one of us (G. H.) by the author and the figures given are taken from that.

be about 54 per cent. These figures in themselves are significant, but even more so are those for patients living useful lives, since about 60 per cent of those whose tumors were entirely removed came into this category but this was true of only some 34 per cent of the patients who had had intracapsular extirpations. These percentages are based on the number of patients living usefully as compared with the total number of patients operated upon.

Aside from the figures from the intracapsular series of Olivecrona, as given by himself and Nielsen, the only chance of making a comparison of this method with that of complete tumor removal is through a study of Cushing's end results as given by several of his pupils, since in practically all instances Cushing's patients were operated upon by the intracapsular procedure. It is because some doubt has existed as to the relative merits of the intracapsular versus the complete extirpation of these tumors that the present study has been undertaken. There are three principal questions to be answered. First, what is the immediate operative mortality in the two groups; second, what is the mortality after an interval of five years, and third, most important of all, what is the percentage of useful survival of the patients operated upon by the two methods?

In respect to the last question, it was mentioned previously that heretofore the percentage of patients in useful life has been based frequently on the number of those who survived the operation as well as a postoperative period, usually of five years. This method, however, would be quite unfair in the present comparison for the reason, as will be pointed out, that whereas the actual operative mortality may be more or less comparable in the two groups, nevertheless, during the next five years a very large number of patients in the intracapsular group will have died, but only an insignificant number of those whose tumors were totally removed. In other words, let us say that there were 100 patients who had been operated upon by the intracapsular method, and at the end of five years, 50 of these patients had died either postoperatively or within this interval. If 25, or half of these survivors, were living useful lives the percentage of useful life based only on the number of survivors would be 50 per cent, whereas if based on the original 100, it would be 25 per cent.

On the other hand, if 100 patients had had their tumors completely removed and only 20 of these had died postoperatively or during the five-year interval with 40, or half the remainder, in useful life, the incidence of useful living based only on the number of survivors would again be 50 per cent even though there were 40 such patients by this method against 25 by the intracapsular procedure, but based on the original 100 patients the figure would be 40 per cent against 25 per cent by the incomplete method. The real question to be decided is, given a certain number of patients having acoustic tumors, what percentage of that original number may be expected to have survived each type of operation and a five-year interval and to be living useful lives at the end of that time or longer?

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RESULTS OF INTRACAPSULAR EXTIRPATION (CUSHING'S SERIES)

The mortality figures here given are taken from Eisenhardt's follow-up report in 1935. The figures for estimated useful survival were derived from reports made on a consecutive three-year series of Cushing's cases by three of his pupils, Van Wagenen,¹² Cairns¹ and Davidoff.⁶

Total patients operated upon (circa 1906-1932).....	176	
Total patients living five years or more.....	77	
Five-year mortality (99 cases including postoperative deaths) ..		56.2 per cent
Useful survival of the total 176 cases.....	44 or 25	per cent
Useful survival of the 77 five-year survivors.....	44 or 57.1	per cent

In reviewing the above statistics it must be remembered that many of Cushing's patients were operated upon in the very early days of neurosurgery when the modern adjuncts of electrosurgery and strong suction and antibiotics were not available, but even so his actual operative mortality was exceedingly low, and was reduced in his last 50 cases to 4 per cent. However, the really significant figure is the one which shows that of the original 176 patients only 77 had survived the operation and the subsequent five-year period. So far as the useful survival of the patients in Cushing's series is concerned the figures are admittedly estimated, but these estimates were taken from follow-up studies by his pupils who were at some pains to get an accurate idea of what the patients' disabilities were, if any. To the best of their knowledge about one quarter (25 per cent) of the 40 patients who were followed were living useful lives, but in view of the statistics given by Nielsen and Olivecrona for the intracapsular operation it is altogether probable that this figure should be raised to 33 to 35 per cent, inasmuch as it is undoubtedly true that Cushing's results by this procedure were at least as good if not better than others using this method. Even so, such a percentage falls far short of that for patients who have had their tumors completely removed.

Since no definite estimate of useful survival can be derived from Dandy's publications, and since it was impossible for Olivecrona to follow a considerable number of his patients on account of war conditions, we have attempted to make a comparison of the intracapsular results of Cushing with our own series of total tumor extirpations. We have considered that patients were living useful lives if they had returned to their original occupation or something comparable to it, or, in the case of women, if they had resumed their usual household duties. Certain older patients who came within the retiring age were considered in useful life if they had no great physical disabilities. However, if patients had handicaps such as marked ataxia or weakness, or if they were blind, even though their vision had been lost before the operation, they were not put into the useful category.

At this point the question of facial paralysis comes up. With but few exceptions, possibly four in our experience, this is almost inevitable in doing a complete extirpation of acoustic neuromas of any considerable size. In the majority of cases the enlarged internal auditory meatus is filled with tumor

cells, and since these must be curetted out, the facial nerve can only in rare instances be spared. This matter has always been discussed with patients, and in all but one case they have preferred this to a recurrence of their growth. The appearance of the face can be helped considerably by a subsequent anastomosis with either the hypoglossal or the spinal accessory nerve. Only when the facial paralysis prevented them from doing some gainful work has this feature been considered as depriving them of useful life.

Since 1934, when we began to do complete extirpation of acoustic tumors routinely, there have been 83 patients so operated upon. However, as mentioned earlier, nine of these patients had been operated upon elsewhere previously with incomplete tumor removal, and these need not be considered here as they present very great difficulties and hazards. Likewise, two patients having bilateral tumors have been excluded for obvious reasons. There were, therefore, 72 patients who had not been operated upon previously and whose tumors were totally extirpated. There were eight deaths in this group, or an operative mortality of 11.1 per cent. Even though none of these patients have as yet died since leaving the hospital, nevertheless in order to get a strict comparison with Cushing's as well as with other series, we shall consider only the 47 patients operated upon from 1934 through 1944, so that a five-year or more follow-up period may be obtained. These data may be summarized as follows.

Patients previously unoperated upon who have had complete removal of their acoustic tumors			
Total patients operated upon (1934-1944).....	47		
Total patients living five years or more.....	41		
Five-year mortality (same as operative mortality).....	6	12.7 per cent	
Useful survival of the total 47 cases.....	31	65.9 per cent	
Useful survival of the 41 survivors.....	31	75.6 per cent	

DISCUSSION

From the data which we have been able to gather through a study of our own series and the other available sources there would seem to be little to say in regard to the merits of the two methods here compared since the figures speak for themselves. In other words, if one compares the above figures or the ones given previously for total tumor removals with the results following the intracapsular operation, it will be seen that the five-year mortality (including postoperative deaths) for patients having complete removals runs from about 12 to 25 per cent, while for the intracapsular it is 53 to 56 per cent. Furthermore, of the original number of patients operated upon, some 60 to 65 per cent with complete tumor removal will be in useful life against possibly 35 per cent of those who have had the intracapsular operation.

There can be no question that any operation on an acoustic tumor is a difficult and somewhat hazardous procedure, but with patience and care they can now be removed completely in the vast majority of instances. If this is done, the patient will not only have as good a chance of coming through the operation as by the old intracapsular method, but will also have an infinitely greater chance of living a permanently useful life.

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The one most serious drawback to the complete operation is the almost certain facial paralysis, but this can be improved to some extent by an anastomosis, and in our experience every patient with one exception has preferred this disability rather than to be faced with a recurrence of the tumor and a far more serious secondary operation. Olivecrona was able to spare the facial nerve in 15 out of 23 complete extirpations (Nielsen) but this is a much higher percentage than we have found possible. It may be that the sitting position which, of recent years, has been employed for this operation may make it easier to identify and save this important structure.

SUMMARY

A statistical study of the end results following intracapsular and complete removal of acoustic tumors has been made from our own material and from such other sources as are available. The five-year mortality rate for the intracapsular operation is well over 50 per cent whereas for the patients who have had complete tumor removals it is from 12 to 25 per cent. About one-third of the patients with intracapsular removals will be in useful life after five years and about two-thirds of those from whom the tumors have been totally extirpated.

The one great disadvantage of the complete operation is a high incidence of facial paralysis, but practically all patients in our own series have preferred to have this rather than a recurrence of their tumors.

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DISCUSSION.—DR. FRANCIS C. GRANT, Philadelphia, Pa.: This is an excellent series of cases which Dr. Horrax and Dr. Poppen have shown us. I think it proves beyond very much question that it is better to attempt to remove these tumors completely than to do a subcapsular enucleation. The mortality is lower after complete extirpation, and all chances of recurrence are avoided. It is true that these tumors grow very slowly and that, therefore, recurrence after subcapsular enucleation may be a matter of years. Nevertheless, they always do recur, and complete cure can only be afforded by complete extirpation.

There are two points in the surgery of these tumors which must be considered. In the first place, every effort must be made to avoid injury to the ninth and tenth nerves, which lie at the lower pole of the tumor. If these nerves can be dissected from the capsule of the tumor without damage, complete extirpation can be done with reasonable safety.

Secondly, if the brain stem, against which the tumor is almost always plastered, is damaged during the removal of the lesion, again, very serious postoperative complications can result. In our experience the most serious postoperative complication is difficulty in swallowing, whether this be due to damage to the vagus or to damage to the brain stem. Aspiration pneumonia is a very common sequela, if the swallowing function is reduced.

In our series of cases in which complete removal was possible, 32 cases have survived from one to five years; 21, from six to ten years; 6, from eleven to fifteen years; and 6, for over fifteen years. Of these 65 patients, 42 are well and working. The other 23 had sufficient neurologic deficit to prevent return to their original occupation.

I was particularly impressed with Dr. Horrax's low mortality. If the mortality can be maintained within reasonable limits and the tumor completely removed, there is no doubt that complete extirpation should always be attempted in acoustic tumors.

DR. HOWARD C. NAFFZIGER, San Francisco, Calif.: I think this paper has given the neurological surgeons a real mark to shoot at. I don't know of any carefully reported series with as creditable results.

I think the method of analysis that Dr. Horrax has used, including operative mortality with five years' useful survival, is really the best sort of criterion. Unfortunately, these patients come to the neurological surgeon late, and, as in the illustration by Dr. Grant, practically every one that we see comes at a stage in which the tumor is large enough to indent the pons.

In the early days the so-called partial removals were not much more than biopsies. A partial removal is a rather loose term, because I think many of us have had the experience of a fatality after what we considered a pretty satisfactory partial removal, but have been appalled to find that we have only nibbled out a very small portion. Unless the removal is considerable, intracranial pressure persists after operation, and the duration of life is quite short.

The future of these people is such that if they are not killed by the tumor they have a considerable expectation of life. In going over the last seventy patients of ours I have found that their average age was 41.8 years, which means that many of them are a good deal younger than that.

There are two points I would like to make: I think the reports in the literature are quite infrequent as to the results of partial and total removal; many of us are not very proud of our results and are inclined not to say too much about them.

In this particular series reported, I think you have heard what can be done by two extraordinarily skillful surgeons working together.

I am not at all sure in my own mind but that the mortality in the hands of the same surgeons is lower in the case of total removal than in the case of partial removal.

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I think the portions left and the sequelae that go with it contribute very largely to the mortality.

I believe this was a perfectly splendid paper.

DR. COBB PILCHER (Nashville, Tenn.): As in the case of many other conditions with which we have to deal, such as carcinoma of the stomach, which has been discussed today, it is unwise to make arbitrary rules; and I should like to point out that each case of acoustic tumor should have a decision made on its own merits as to whether or not a complete or an intracapsular removal should be done.

In a young person with many years to live certainly the radical removal is well justified. On the other hand, we know that many of these patients are in advanced years at the time they are first seen. The duration of symptoms, for which I have no accurate statistics, but which I would guess to be not less than an average of ten years, indicates the slowness of the growth of the tumor, and suggests the slowness of its recurrence.

Certainly in an elderly person, in whom the risk of damage to the pons, of damage to the blood supply of the brain stem, and risk of facial paralysis and, may I say, also of the fifth nerve destruction which almost always goes with facial paralysis, I would consider that an intracapsular enucleation, by which I mean removal of almost all of the capsule except the small tab in the pars acousticus, is preferable. Let us not make dogmatic rules to cover all cases.

DR. GILBERT HORRAX (Boston, Mass.): I want to thank these gentlemen for their very kind discussion of this paper.

Dr. Naffziger has touched on one point which I should have mentioned in my original giving of the paper, which I did not have time to do, and it is this: I feel greatly indebted to Dr. Poppen for his contributions to this paper, because it was he who in the first place urged me to take up the complete enucleation of these tumors, because I had been brought up in the school that thought the intracapsular procedure was the only thing to do. Dr. Poppen played the major role very often, and I want to give every credit to him for the results we have had.

In regard to what Dr. Pilcher said, he is quite right that one must bear in mind the occasional case of elderly individual who might do well with intracapsular enucleation of the particular kind he mentioned. I would call that, however, a subtotal enucleation, a term such as Dr. Olivecrona uses in describing his procedures—the complete, the subtotal and the intracapsular. Even in the best of hands, such as Dr. Cushing and Dr. Olivecrona, when the operative mortality is well over 50 per cent after five years, I don't see that there is any real question as to which is the best procedure in the vast majority of cases.

ERRATUM

Due to typographical error in Table I of the article titled "Disarticulation of an Innominate Bone for Primary and Metastatic Cancer," on page 96 of the July, 1949, *ANNALS OF SURGERY*, appeared the statement under remarks concerning patient No. 8 "Patient well 14 months after surgery." The length of time should read four months.

STREPTOMYCIN, AUREOMYCIN AND CHLOROMYCETIN: EXPERIMENTAL AND CLINICAL COMPARISON*

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AND

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Repeated reports have demonstrated the effectiveness of penicillin, streptomycin and the sulfonamides in peritonitis. In addition, preoperative use of these agents has been found to be of value in reducing the incidence of peritonitis in those surgical conditions in which, in the past, it has been relatively high.

Domagk¹ demonstrated the value of sulfonamides in the treatment of peritoneal infections in mice. Bower² and his associates tested the effects of prontosil on the mixed type of peritoneal infection commonly seen in human peritonitis, while Epps³ and his associates compared the merits of sulfanilamide and sulfathiazole. Fauley *et al.*⁴ studied the influence of penicillin in experimental peritonitis in dogs. Crile,⁵ in a clinical study, reported the results of treatment with penicillin of peritonitis of appendiceal origin.

Murphy, Ravdin *et al.*⁶ have studied the effects of streptomycin in experimental peritonitis in dogs, and, in addition, have shown that it passes into the peritoneal cavity, and frequently reaches a higher concentration than in the blood.

Kay and Lockwood,⁷ in their experimental studies, expressed the thought that peritonitis is a systemic disease. This was based on their gross and microscopic findings at autopsy. They believed that changes in prothrombin time might be of prognostic value.

Pulaski,⁸ in analyzing a series of clinical cases with peritonitis, stated that streptomycin, used alone, is especially effective in spreading and in localized types of peritonitis without a palpable mass. In a personal communication, he states that treatment of early spreading peritonitis with streptomycin and penicillin combined, seems to offer no significant advantage over streptomycin alone. He states, however, that in the management of localizing lesions, combined therapy seems superior.

Several additional antibiotics have been developed since the discovery of penicillin and streptomycin. Bacitracin, aureomycin and chloromycetin are representative of this new group. Bacitracin, which has been found to be effective in staphylococcal and streptococcal infections, was not considered pertinent to this study.

Aureomycin,[†] which is derived from a strain of *Streptomyces aureofaciens*,

* Read before the American Surgical Association, St. Louis, Mo., April 21, 1949.

† This study was aided by a grant from the Lederle Laboratories Division, American Cyanamid Company.

has been shown to possess, in vitro, antibacterial activity against numerous gram-positive and gram-negative bacteria. It appears to be bacteriostatic rather than bactericidal, except in high drug concentrations.

Chloromycetin,* which is obtained from filtrates of submerged aerated cultures of a *Streptomyces* sp., has been found to be quite effective against a number of rickettsiae, and several gram-negative bacteria. In vitro, crystalline chloromycetin has been found to be inactive against yeasts and filamentous fungi, inactive against protozoa, moderately active against gram-positive bacteria and *Mycobacterium tuberculosis*, and active against gram-negative bacteria and *Borrelia recurrentis*. Among the gram-negative organisms showing a considerable degree of sensitivity are the *Brucellae*, members of the salmonella group, and coliform bacteria.

TABLE I.—Comparative Sensitivity of Organisms Commonly Found in Peritonitis of Appendiceal Origin.

Organism	Penicillin	Streptomycin	Aureomycin	Chloromycetin
<i>Staph. non hemolyticus</i>	Excellent	Moderate	Excellent	Moderate
<i>Str. viridans</i> , alpha	Excellent	Not susceptible	Excellent	
<i>Str. pyogenes</i> , beta	Excellent	Moderate	Excellent	
<i>Str. non hemolyticus</i> , gamma	Excellent	Moderate	Excellent	Good
<i>Escherichia coli</i>	Not susceptible	Good	Excellent	Moderate
<i>Clostridia</i>	Moderate	Not susceptible		
<i>Proteus</i>	Not susceptible	Moderate	Not susceptible	Excellent
<i>Strept. faecalis</i>	Excellent	Good	Moderate	

Both aureomycin and chloromycetin are well absorbed from the gastrointestinal tract. There are no reports up to the present time of toxic manifestations resulting from the oral administration of chloromycetin. Aureomycin has low toxicity. Nausea and gastro-intestinal irritation, manifested by diarrhea, has been reported.

The influence of both is greatest on the rickettsiae and on the viral agents of the psittacosis-lymphogranuloma group. Their in vitro and in vivo range of activity closely approximates one another. However, unlike chloromycetin, most strains of gram-positive cocci, pneumococci and hemolytic streptococci are actively inhibited by aureomycin.

Woodward,¹⁵ in a presentation at the General Session, American College of Physicians, March 30, 1949, reported the therapeutic effects of these two new antibiotics in typhoid fever, undulant fever, tularemia, scrub typhus, murine typhus, rocky mountain spotted fever, as well as epidemic typhus and Q fever. He believes that chloromycetin is clearly the drug of choice in clinical

* The chloromycetin used in this study was supplied by the Research Division, Parke, Davis & Company.

typhoid. In tularemia, he states that aureomycin is more effective than streptomycin. Chloromycetin has not been tried clinically in tularemia. Experimentally, it is less effective than streptomycin.

Aureomycin has been found to be of value in lymphogranuloma venereum, psittacosis and primary atypical pneumonia. Comparison in these conditions with chloromycetin awaits further clinical trial.

In comparing the range of bacterial sensitivity of aureomycin and chloromycetin with streptomycin and penicillin (Table I), it seemed that valuable data might be obtained by studying the individual effectiveness of each of these antibiotics in a mixed type of infection such as occurs in peritonitis. Since peritonitis, in dogs, is comparable to human peritonitis, it was decided to study the effects of each of the four enumerated antibiotics in an experimental study on this animal.

Peritonitis was produced by two methods in this investigation. One employed the technic introduced by Bower and co-workers, and as modified by Fauley and his associates; the second, which basically represents a second study, employed the technic suggested by Rothenberg, Silvani and McCorkle.¹⁹ These will be described as Study I and Study II.

STUDY I

Animals were selected at random from stray, mongrel adult dogs weighing from 15 to 20 pounds and excluding pregnant dogs, and dogs previously operated upon. The abdomen was shaved, scrubbed and painted with iodine and alcohol. Aseptic technic was rigidly observed. Under intravenous nembutal sodium anesthesia, the abdomen was entered through a right rectus incision and the appendix drawn into the wound. Mesenteric attachments were divided, and the appendiceal vessels were clamped, divided and ligated with silk. In order to minimize a tendency toward intussusception, the appendix was ligated 1 cm. from its base, with three coarse silk ties, rather than directly at its base. The distal half of the appendix was then traumatized with a crushing clamp, the viscera replaced, and the incision closed in layers with silk. No drains were used and no dressings applied. Immediately after operation, each animal received 50.0 cc. of castor oil by stomach tube.

No attempt was made to withhold food or water postoperatively, and no intravenous fluids were given. Temperature and leukocyte counts were determined every other day. Necropsy was performed on all fatalities shortly after death. All animals operated on are included in the series. The animals that survived were examined not earlier than 14 days after operation. Bacterial culture studies were made of peritoneal exudate in all animals. A combination of antibiotics was not used in any of the treated animals, although it was recognized that their effectiveness might have been enhanced thereby. The purpose of the study was to compare the results of the antibiotics individually. Penicillin was not used in Study I.

Ten animals were used as controls. Of these, eight died of acute diffuse

STREPTOMYCIN, AUREOMYCIN AND CHLOROMYCETIN

peritonitis, six of them within the first four days. Two animals recovered, a survival rate of 20 per cent.

Ten animals were treated with streptomycin, starting 24 hours postoperatively and continuing for eight days. The dosage was 75 mg. every six hours intramuscularly, a dosage equivalent of 300 mg. every 24 hours. Of these, four died of peritonitis, three of them within the first six days. Six animals recovered, a survival rate of 60 per cent.

Ten animals were treated with aureomycin, starting 24 hours postoperatively and continuing for eight days. The dosage was 100 mg. four times a day orally. Of these, only one animal died, this occurring as late as the ninth day. Nine animals recovered, a survival rate of 90 per cent.

Ten animals were treated with chloromycetin, starting 24 hours postoperatively and continuing for eight days. The dosage was 62.5 mg. every four hours orally. Of these, two animals died, one on the fourth day, and one on the eighth day. Eight animals recovered, a survival rate of 80 per cent.

TABLE II.—(Study I) Comparison of the Survival Rate in the Treated and Untreated Animals.

	No. Dogs	2-Day Survivals	4-Day Survivals	8-Day Survivals	14-Day Survivals
Controls.....	10	8	6	4	2
Streptomycin.....	10	10	8	6	6
Aureomycin.....	10	10	10	10	9
Chloromycetin.....	10	10	9	8	8

All animals were autopsied as soon after death as possible, and peritoneal exudate culture studies made. In addition, all dogs that survived 14 days were sacrificed and culture studies made. Five control animals showed a predominance of *Escherichia coli*. Eight animals treated with streptomycin showed *Escherichia coli*, while only four treated with aureomycin showed this organism. It is interesting to note that of ten animals treated with aureomycin, eight showed various types of proteus organisms. All ten animals treated with chloromycetin showed *Escherichia coli*, while only two showed proteus organisms.

The comparative survival rates of Study I are shown in Table II. The results of bacteriological studies* of peritoneal exudate are shown in Table III. Note that only five of the ten control animals showed *Escherichia coli*, while eight out of ten animals treated with streptomycin, and ten out of ten treated with chloromycetin showed this same organism. Four control animals revealed proteus organisms; only two each of those treated with streptomycin and chloromycetin showed proteus organisms, while eight out of ten treated with aureomycin showed this organism.

* Grateful acknowledgment is made to Dr. Frank W. Hachtel, Professor of Bacteriology, University of Maryland School of Medicine, and Miss Audrey Funk, Bacteriologist, University Hospital, Baltimore, Maryland.

STUDY II

Rothenberg *et al.* have suggested that a more effective method of producing peritonitis in dogs would be to combine excision of the spleen and omentum with the technic of Bower, Fauley *et al.* as described under Study I.

Under Study II, the same principles of technic were observed except for the following: (a) In addition to isolating and ligating the cecum, the spleen

TABLE III.—(Study I) Incidence of Bacteria Cultures from Peritoneal Exudate of Dogs, with Experimental Peritonitis.

Organism	Incidence	Controls 10 Dogs	Streptomycin 10 Dogs	Aureomycin 10 Dogs	Chloromycetin 10 Dogs
<i>Escherichia col.</i>	5	8	4	10	
<i>Gamma streptococcus</i>	4	5	3	3	
<i>Proteus</i>	4	2	8	2	
<i>Clostridia perfringes</i>	5	3	1	7	
<i>Staphylococcus albus</i>	4	0	0	1	
<i>Streptococcus viridans</i>	0	2	0	5	
Beta hemolytic <i>streptococcus</i> ..	1	2	0	5	
<i>Staphylococcus aureus</i>	2	0	0	0	

and the omentum of each animal were excised; (b) Five animals were used in each series instead of ten, and the period of observation covered seven days instead of 14. This shorter period of observation was selected because we were interested in bacteriological studies of peritoneal exudate rather than survival rate. The survival study is shown in Table IV.

TABLE IV.—(Study II.) Comparison of the Treated and Untreated Animals in Experimental Peritonitis. (Method as in Study I with addition of excision of spleen and omentum).

Group	1st Day	2nd Day	3rd Day	4th Day	5th Day	6th Day	7th Day
Control.....	5	5	4	4	3	3	3
Streptomycin....	5	4	4	4	4	4	4
Penicillin.....	5	5	5	5	5	5	5
Aureomycin.....	5	5	5	5	5	5	5
Chloromycetin....	5	5	5	4	4	4	4

Five animals were used as controls, of which three survived seven days. All five animals showed a generalized peritonitis at autopsy, and no tendency to wall off. Eight different types of organisms were cultured from the peritoneal exudate with a total incidence of 22 positive cultures.

In this same study (Study II) the effects of penicillin were observed, in addition to those of streptomycin, aureomycin and chloromycetin. All five animals treated with penicillin survived for seven days, and then were sacrificed. Two of these animals showed a diffuse peritonitis and three showed a well localized abscess without evidence of a diffuse peritonitis. Bacteriological studies of peritoneal exudate revealed four different strains of organisms. The total incidence of positive cultures was eight. Five of these showed a heavy

over-growth of *Escherichia coli*. This represents the maximum number of positive cultures possible to attain in this study for any specific organism.

Four animals treated with streptomycin out of a possible five survived seven days. Autopsy of the animal that did not survive showed a diffuse peritonitis. Of those that survived, one showed a diffuse peritonitis, and three showed localized abscess formation about the appendiceal stump without evidence of diffuse peritonitis. Bacteriological studies revealed four types of organisms with a total incidence of 11 positive cultures.

TABLE V.—(Study II.) *Postmortem Peritoneal Findings.*

Group	Animals not Surviving 7 days		Animals Surviving 7 days	
	Diffuse Peritonitis	Local Abscess	Diffuse Peritonitis	Local Abscess
Control.....	2	0	3	0
Streptomycin.....	1	0	1	3
Penicillin.....	0	0	2	3
Aureomycin.....	0	0	2	3
Chloromycetin.....	1	0	4	0

All five animals treated with aureomycin survived seven days. Upon sacrificing, autopsy studies revealed two with a generalized peritonitis, and three with localized abscess without evidence of diffuse peritonitis. Four types of organisms were cultured with a total incidence of 11 positive cultures. This incidence is similar to that for streptomycin, although the strains of organisms cultured were different. Streptomycin and aureomycin each had only one positive culture for *Escherichia coli*.

TABLE VI.—(Study II.) *Organisms Cultured from Peritoneal Exudate of Treated and Untreated Animals.*

Organism	Control	Strepto- mycin	Peni- cillin	Aureo- mycin	Chloro- mycetin
<i>Streptococcus hemolyticus</i>	3	..	1	2	1
<i>Streptococcus non-hemolyticus</i> ..	3	3
<i>Streptococcus viridans</i>	4
<i>Escherichia coli</i>	4	1	5	1	3
<i>Staphylococcus albus</i>	2	3	1	..	2
<i>Clostridia</i> group.....	5	3	1	..	4
<i>Proteus vulgaris</i>	2	4	2
<i>Streptococcus faecalis</i>	2	4	..
Gram negative rod anaerobe...	1

In the series of animals treated with chloromycetin, four out of five survived. The animal that did not survive showed a diffuse peritonitis. In addition, the four animals that were sacrificed at the end of seven days, also showed a diffuse peritonitis. Bacteriological studies of the peritoneal exudate were positive for six types of organisms with a total incidence of 15 positive cultures. *Escherichia coli* was cultured in three out of five instances, and *Proteus vulgaris* appeared twice.

The character of peritonitis found at autopsy is shown in Table V, and the results of bacteriological studies in Table VI.

CLINICAL STUDIES*

Since making our preliminary report, additional data has been accumulated, indicating the clinical applicability of aureomycin from the surgical viewpoint.

Eleven patients, with an age range of one and one-half to 39 years with generalized peritonitis secondary to perforation of the appendix have been treated with aureomycin. *Escherichia coli* cultures were obtained in nine of the 11 cases. In the remaining two cases, positive cultures were obtained for beta-hemolytic streptococci and *Clostridium welchii* respectively. Each patient was surgically treated by the removal of the appendix. Drainage was established in all of these cases. There were no deaths. The average length of stay in the hospital was 14.9 days.

Two patients with localized peritonitis secondary to perforation of the appendix also were treated with aureomycin. The appendix was removed in each case, and the abscess drained. The ages were four years and 71 years respectively. The average stay in the hospital was 9.9 days.

One patient, age 52, with a ruptured sigmoid diverticulum and generalized peritonitis, was treated by cecostomy, drainage of the peritoneal cavity and aureomycin. Peritoneal cultures revealed micro-aerophilic *Streptococcus viridans*. This patient died on the eleventh postoperative day. In view of the subsequent culture, it is possible that aureomycin combined with penicillin would have been of greater value.

Three patients with clinical evidence of an acute inflammatory reaction in the peritoneal cavity were treated with aureomycin and non-surgical intervention. One patient subsequently had an interval appendectomy. The appendix showed definite evidence of having been perforated. The history in each instance suggested a diagnosis of acute appendicitis with spreading peritonitis. The objective findings supported this impression. A brief summary of these three cases follows.

Case 1. W. T., No. 21376. This was a colored male, age 4, admitted to the University Hospital on February 9, 1949, with a history of pain in the left lower abdomen of 2 days duration. The pain had been severe and cramplike in character and associated with vomiting. Enemas had been moderately effective, without evidence of blood or mucous.

Admission temperature was 101.2° F. and leukocyte count 11,500. There was muscle splinting of the entire abdominal wall with board-like rigidity in the left lower abdomen. Tenderness was extreme in the left lower quadrant, and moderate elsewhere. Peristalsis was audible over the entire abdomen, except in the left lower quadrant. Rectal examination confirmed the impression of a mass in the left pelvic region. A tentative diagnosis of an abscess in the left pelvic region was made.

He was immediately given 50 mg. of aureomycin intramuscularly, and then placed on a regimen of 25 mg. of aureomycin intramuscularly every 4 hours, supplemented with

* Grateful acknowledgment is made to Drs. William D. Lynn and Thomas G. Barnes, University Hospital, Baltimore, Maryland.

an oral dose of 500 mg. every 6 hours. At the end of 6 days, parenteral medication was discontinued and the oral dose of aureomycin was reduced to 250 mg. every 6 hours. This therapeutic level was continued for 3 days, following which aureomycin therapy was discontinued.

Thirty-six hours after admission, abdominal tenderness had disappeared except in the left lower quadrant. Fifty hours after admission, there was but slight tenderness in the left lower abdomen and a mass, which shortly after admission became well defined in this area, appeared to be regressing rapidly.

Fourteen days after admission, he was discharged from the hospital with negative physical findings.

On April 5, 1949, he was readmitted to the University Hospital for an elective exploratory laparotomy. During the interval of discharge and readmission, he had remained asymptomatic.

Exploratory laparotomy following this admission revealed a mobile caecum, pulled somewhat to the left. The appendix, which was about 4 cm. in length, extended transversely across the pelvic brim, and was adherent to the superior surface of the bladder and peritoneum of the left iliac region. Loops of ileum were adherent anteriorly. Adhesions were friable. No free pus was encountered. The middle third of the appendix was about 1 cm. in diameter, and contained a thick exudate. The appendix was removed, and the stump invaginated. Convalescence was entirely without event.

Case 2. W. R., No. 45179. A white male, age 30, was admitted to the University Hospital on March 6, 1949, complaining of lower abdominal pain of 11 hours duration. He had been under medical care since 1941 for chronic infectious hepatitis. At the time of his present admission, he was convalescent both from a recent exacerbation of hepatitis and a liver biopsy.

On admission, the patient was slightly icteric. His most recent liver function test revealed a direct van den Bergh of 4.8 and an indirect one of 4.5. Bromsulfalein 28 per cent at the end of 40 minutes. Total proteins were 6.30, with an A-G ratio of 4.20 to 2.10. Physical examination revealed tenderness in the left lower quadrant just to the left of the midline, as well as marked tenderness and muscle spasm in the right lower quadrant in the area of McBurney's point. Rebound tenderness was present. No masses were palpated. Admission temperature was 101° F.; leukocyte count 14,700. In view of the evidence of severe recurring hepatitis, conservative therapy was advocated. He was placed on an oral dosage of 500 mg. of aureomycin every 4 hours, and the abdomen was re-examined every hour. In 12 hours, the temperature had dropped to 99.8° F., and the leukocyte count to 10,900, and in 24 hours, the temperature was 98.0° F., with a leukocyte count of 8,850. Simultaneously, there was a dramatic amelioration of signs and symptoms in the abdomen.

Thirty-six hours after admission, the blood count was 7,650 with a normal temperature. He was discharged from the hospital on the fourth day after admission. Total dosage of aureomycin 8 Gm. which was not supplemented with other antibiotics or chemotherapeutic agents. Five week follow-up has revealed no sequelae.

Case 3. M. W., No. 43960, a white female, age 56, was admitted to the University Hospital on January 15, 1949, with a history of pain in the lower abdomen of two days duration, which had become excruciating 6 hours prior to admission. The pain, which was cramplike in character, radiated from the right lower quadrant into the left lower quadrant. There was no history of constipation or vomiting.

Admission temperature was 100.8° F. and the leukocyte count 24,300. Urinalysis was negative. There was marked tenderness and rigidity in both lower quadrants of the abdomen, and moderate tenderness in the upper quadrants. Pelvic examination was negative, except for tenderness in the right pelvic region.

A diagnosis of peritoneal irritation, probably secondary to an acute appendix, was made. Exploratory laparotomy was advised but was refused by the patient.

She was given 300,000 units of penicillin immediately after admission. This was repeated in 12 hours.

Twenty-four hours after admission, her temperature was 101° F. and abdominal rigidity was more marked in the right lower quadrant. She persisted in refusing operation. Penicillin was discontinued and she was given 1 Gm. of aureomycin orally. This was followed by 500 mg. of aureomycin every 4 hours. Approximately 14 hours later, her temperature was 99.5° F. and leukocyte count was 17,000. She was subjectively improved. Abdominal tenderness had diminished.

Thirty-six hours after starting aureomycin therapy, a mass could be palpated in the right lower abdominal quadrant, about the size of an orange. On the third day of therapy, she was afebrile and asymptomatic. Abdominal tenderness had disappeared and the mass had reduced in size. Leukocyte count was 11,000. She was discharged two days later, completely asymptomatic, at which time the mass in the right lower quadrant had become poorly defined. Follow-up has not been possible.

DISCUSSION

The evidence in Case 3 supported a diagnosis of a spreading peritonitis, for which exploratory laparotomy was indicated and advised. Following the patient's refusal of operation and lack of response to penicillin, she was placed on aureomycin. Crile has shown that response to penicillin in peritonitis takes three to four days, and Altemeier²⁴ has offered an explanation for this slowness of response. It is possible that the apparently rapid response to aureomycin is due to its ability to act against *Escherichia coli* as well as secondarily associated organisms.

A total of 13 patients with peritonitis, secondary to appendicitis, were treated by surgery and aureomycin, and three patients with presumptive evidence of peritonitis were treated by aureomycin alone, without a fatality.

In addition, three intractable urinary tract infections, each of which showed positive cultures for *Escherichia coli*, have been successfully treated with aureomycin. Two of the cases are included with Table VII, showing an analysis of the clinical results.

The third case occurred in a 60-year-old male following a left lower pelvic ureterolithotomy. During the course of a year he had repeated hospital admissions because of chills, fever, urinary frequency and urgency. During these admissions he had penicillin, streptomycin and sulfadiazine respectively, without appreciable influence. He was placed on a course of 250 mg. of aureomycin every four hours for eight days, after which bacteriological studies of the urine were negative. He has remained asymptomatic during a five month follow-up period.

Table VII shows the surgical conditions treated with aureomycin, and Table VIII, the types of bacterial organisms cultured.

Chloromycetin has not been given a clinical trial from the surgical viewpoint except in lymphogranuloma venereum. In this condition it will probably compare in value with aureomycin. Experimental data thus far obtained does

not warrant its clinical use in peritonitis. In infections involving proteus organisms, it should prove to be of merit.

Ochsner and Johnston²⁵ have estimated that in cases of appendiceal peritonitis treated conservatively, three-fourths will subside spontaneously without going on to abscess formation, and that in the remaining 25 per cent incision and drainage of the abscess will be necessary.

TABLE VII.—*Clinical Studies.*

	No. Patients	Diagnosis	Av.		Results	Mortality
			Age	Hospital Days		
Non-operative Cases	3	Acute appendicitis	30	5.66	Excellent	0
	2	Acute perforated appendicitis, walled-off abscess	44.5	9.9	Excellent	0
Operative Cases	11	Acute perforated appendicitis, generalized peritonitis	19.42	14.9	Excellent	0
	1	Perforated sigmoid diverticulitis, generalized peritonitis	52	11	Cecostomy and drainage	Died
Post-Operative Genito-Urinary Infections	1	<i>E. coli</i> cystitis, gastric ulcer	74	19	Asymptomatic	Died from severe gastric hemorrhage
	1	<i>E. coli</i> cystitis and peritonitis, following uretero-sigmoidostomy	72	39	Excellent	0
Total	19		23.40	11.21		10.5%

Crile, in discussing a series of cases of peritonitis of appendiceal origin, reported 23 cases that were treated successfully with penicillin alone. Four days of therapy with penicillin was adequate to control the average case. Of the 23 cases reported, 20 subsequently had an interval appendectomy with confirmation of a gross perforation of the appendix.

TABLE VIII.—*Organisms Cultured from Clinical Cases.*

Organism	<i>E. Coli</i>	<i>B. Hemolytic Strept.</i>	<i>Strept. Viridans</i>	<i>Cl. Welchii</i>
Number of cases.....	10	2	1	1

It has been stated by several observers that *Escherichia coli*, in pure culture, is not a pathogenic organism, but is in reality a saprophyte, and that in mixed infections, the gram-positive cocci are the chief offenders. Since penicillin does not inhibit the growth of *Escherichia coli*, its effectiveness in peritonitis is probably due to its ability to control secondarily associated organisms.

Altemeier has shown that cultures of *Escherichia coli* or of *Bacillus pyocyaneus* have the property of destroying the activity of penicillin. This ability could well account for the fact that large doses of penicillin are required to

control gram-positive cocci when they are growing in a mixed infection associated with *Escherichia coli*.

The treatment of peritonitis of appendiceal origin with antibiotics should not be construed as a substitute for surgery. Our series of patients is too small to be of clinical significance. However, the experimental and clinical results obtained suggest that aureomycin has a protective mechanism in peritonitis of appendiceal origin. A combination of penicillin and aureomycin therapy should be extremely effective in the treatment of peritonitis of appendiceal origin in those conditions, where for one reason or another surgery is either contra-indicated or physical (environmental) conditions preclude its possibilities. As a dual adjunct in the surgical treatment of peritonitis of appendiceal origin, it should further reduce the present mortality rate. If sufficient aureomycin is given to destroy the *Escherichia coli*, it is possible that smaller doses of penicillin would be effective.

SUMMARY AND CONCLUSIONS

1. The clinical applicability of chloromycetin and aureomycin is reviewed. The major field of their usefulness appears to be in the treatment of infections with rickettsiae and certain of the virus group, and gram-negative infections.
2. Experimental peritonitis has been produced in a series of dogs in an attempt to compare the protective significance of aureomycin and chloromycetin with streptomycin and penicillin.
3. Experimental animals in Study II treated with either streptomycin, penicillin or aureomycin showed a tendency to develop a localized peritonitis. Control animals and those treated with chloromycetin did not show this tendency.
4. Additional experimental studies with chloromycetin and in larger doses, should be made before its clinical trial in peritonitis of appendiceal origin.
5. Smaller doses of penicillin would probably be adequate in the treatment of mixed infections involving *Escherichia coli*, when combined with aureomycin.
6. Since aureomycin is extremely effective against *Escherichia coli*, as well as most strains of gram-positive cocci pneumococci and hemolytic streptococci, further studies may prove it to be the antibiotic of choice in the treatment of peritonitis of appendiceal origin.

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DISCUSSION.—DR. WILLIAM A. ALTEMEIER, Cincinnati, Ohio: Most surgeons agree that modern chemotherapy has been of great value in the treatment of acute septic peritonitis. There is, however, no agreement as to the most effective antibacterial agent. As yet, there is no specific treatment for peritonitis and successful management depends primarily on early diagnosis and prompt surgical intervention. A review of our clinical experience in a total of 1283 cases of acute secondary peritonitis during the past eight years reveals that the mortality was reduced approximately 60 per cent in the 598 cases treated with

penicillin or penicillin and sulfadiazine. In our experience, streptomycin has been definitely inferior to either penicillin or sulfadiazine in the treatment of this disease.

Experimental work has shown that acute septic peritonitis, secondary to lesions of the gastroenteric tract, is usually a synergistic infection produced by the cumulative action of the various intestinal bacteria, and that nonpathogenic bacteria may be of importance in increasing the virulence of others with which they are associated. We also believe that clinical peritonitis following perforated viscera is not primarily an infection caused by gram-negative bacteria, but a mixed or synergistic infection in which the gram-positive organisms are often and usually more important. Large doses of penicillin are effective in secondary peritonitis because of their inhibitory effect on the gram-positive aerobic and anaerobic bacteria and not because of their action on the gram-negative organisms.

More recently we have become interested in aureomycin and chloromycetin as potentially effective chemotherapeutic agents in peritonitis. Both agents possess antibacterial activity against gram-negative and gram-positive, aerobic and anaerobic bacteria. Our experience with chloromycetin in experimental peritonitis and in a limited number of clinical cases of acute secondary peritonitis suggests that this agent is an effective and valuable agent. As more practical means of administering aureomycin and chloromycetin parenterally are found, the effectiveness of these agents should be increased.

DR. WILLIAM L. BYERLY, Jr., Baltimore, Md.: I would like to express appreciation for such an enlightening discussion by Dr. Altemeier. It is well understood that a secondary fecal peritonitis is the result of a symbiotic relationship of organisms from the lower bowel with a ruptured appendix postoperatively leading to other causes.

(Slide) On this slide are listed the predominating organisms in 14 operative cases of diffuse peritonitis just discussed by Dr. Yeager. It is noted that the most frequent organisms, the colibacillus and the hemolytic streptococcus, have been shown experimentally and in vitro to be very susceptible to aureomycin.

The microphilia *Streptococcus viridans*, as previously mentioned, is not as susceptible to aureomycin, as it is to penicillin; and in the patient, as Dr. Yeager just mentioned, it may have been best if we had used penicillin in conjunction with aureomycin.

Likewise, clostridia organisms have not been found susceptible to aureomycin. We have not been able to make any satisfactory sensitivity determinations of clostridia organisms to aureomycin.

(Slide) However, as shown on this next slide, we do know that penicillin is moderately effective against the clostridia group. This slide shows the comparative sensitivity of the organisms commonly found in peritonitis of appendiceal origin and those which we have found in our experiments. You will notice that the gram-positive organisms are very susceptible to both penicillin and aureomycin. Aureomycin and not penicillin is effective against the gram-negative rods of the coliform group. The clostridia group as well as the *Streptococcus faecalis* are more susceptible to penicillin than to aureomycin.

Another interesting factor is that chloromycetin is the only antibiotic that the proteus group is highly susceptible to.

Early in the day a member of the Association mentioned something about the effect of these drugs on pyocyanic infections. Although it is not a common organism found in peritonitis, we see a number of infections with this organism. In both clinical and experimental studies it has been shown that chloromycetin, as in proteus group, has an excellent effect on this organism.

Editorial . . .

POSTOPERATIVE DEATHS

A SIGNIFICANT FEATURE of surgical progress during recent years has been the progressively lower and lower case fatality rates attained in radical surgery of the colon and rectum, the stomach, the lung, the pancreas and duodenum, and other organs. In each case the mortality rates reported from leading centers were initially high, that is, from 25 per cent to 50 per cent, especially during early developmental stages of the work. However, with increasing technical perfection gained through specialized experience and team-work, the acceptable rates fell year by year. Dr. D. F. Jones, a skillful Boston surgeon who pioneered in the introduction to American surgery of the combined abdomino-perineal resection for cancer of the rectum, lost from immediate operative complications about one fourth of the first hundred Miles operations in his series, commencing in about 1912. Twenty years later, as he approached his retirement, he was able to point with pride to the loss of less than one twelfth of his last hundred cases together with a substantial increase in the resectability rate. This record was established without benefit of sulfonamides and antibiotics, without blood banks and the employment of massive transfusions, without anticoagulant therapy for prevention or treatment of embolic disorders, and without reliance upon a staff of trained residents—and stands as an example of what could even then be attained through the acquisition of wisdom and technical perfection by a conscientious surgeon working without a complex specialized hospital team. The gains of the past 15 years in pre- and postoperative care have not brought about substantial improvement over the best records attained by individual master surgeons of the previous era—but they have gone part-way to reduce the gap between the best and the average. Many teaching hospitals and surgical clinics can now report operative mortality rates of less than eight per cent in most types of major cancer surgery, with many of the operations being performed by trained residents who are only at the threshold of their professional careers. In fact, the provision of team-work through the graduated residency system is probably of major significance in recent progress.

There is some danger that an attitude of complacency toward the risks of major surgery may be developing, based on the assumption that adequate supportive treatment (often to be given by some assistant) will offset all of the technical imperfections of a poor operation. This attitude must be vigorously combatted in all of the centers of training, because, far from being satisfied with our present records, we must continue to strive toward the virtual elimination of operative fatalities. If we face the matter honestly, we should recognize that we possess at this time the *knowledge* and the *technics* to guarantee a better than fifty-to-one chance for survival to every patient subjected to major surgical procedures. That we do not yet meet this standard is

due more to human error in not applying all available knowledge than to the occurrence of events beyond possible prevention or control.

Therefore, an important avenue for clinical research is the unremitting and exhaustive analysis of the factors contributing to each death which occurs as a consequence of the operation, rather than as a direct result of the patient's disease. If the death is due to the anesthesia, and fortunately such deaths are rare, there was probably a failure to maintain proper balance between oxygen intake and dose of anesthetic. If the death is due to shock, or renal or hepatic dysfunction, there was probably failure to provide adequate and proper hemostasis and/or blood replacement, or else the patient's pre-operative depletion was not sufficiently compensated. If a catastrophic embolus is responsible, we may have failed to recognize early phlebothrombosis in a peripheral vein and thus missed the opportunity to supply appropriate preventive measures. If death has occurred from pulmonary complications, we must ask ourselves whether we have given the patient the fullest benefits of tracheal suction, antibacterial therapy, the maintenance of full ventilation, and proper fluid management. If peritonitis or ileus has supervened, we must suspect technical errors at the time of operation, inadequate bowel decompression, or sins of omission or commission in connection with nutritional fluid, or electrolyte balance. Since in this day and age the patient will certainly have been saturated with antibiotic agents, omission of the latter will probably not have been a contributing factor! This list of avoidable causes for operative deaths could be extended far enough to leave us with very few factors in mortality which are necessarily beyond our powers of control, but there are some areas in which active research should still be conducted, such as:

1. Improvement in our understanding of the effects of anesthesia and operation on hepatic and renal functions and of ways of offsetting such effects.
2. Better technics for rapid restoration of the debilitated patient so that the effects of operation will be better tolerated. A really complete parenteral feeding regimen, allowing up to 4000 calories per day, together with amino acids, and all of the necessary electrolytes and vitamins would be of great assistance to this end.
3. Some means for preventing thrombotic complications without the necessity to resort to drastic anticoagulant therapy.
4. Adaptation of methods of maintaining the stable state to the special requirements of aged patients.

However, the greatest need in this area of operative mortality is not for research so much as for insistence on education in, and consistent practice of *knowledge which is already available*. If it were generally known that two hospitals can exist within a radius of five miles in which the mortality risk for a major abdominal operation is approximately twenty times as great in one as in the other, there would not be as much self-satisfaction within the profession as there seems to be.

POSTOPERATIVE DEATHS

The surgeon who frequently travels by plane may have experienced the disquieting realization that the responsibility of pilot to passenger is quite analogous to that of surgeon to patient. Without having had any basis for judging the pilot's personal qualifications for the job, apart from the position his employers have given him, the passenger has staked his life on the pilot's ability to apply his technical judgment and skill to the handling of that airplane. He is counting upon him to bring the plane successfully through any unexpected and dangerous situation which may arise in flight. Since it is said that 80 per cent of airplane accidents are due to pilot-error, it is essential that the pilot *make no mistakes*. A major difference between responsibility of pilot and surgeon is that the former shares directly in the consequences of his error or neglect, while the latter does not. The least the surgeon can do is to learn all he can from each failure, whether it be his or another's, and to keep to a minimum those mishaps which could be said to be due to "pilot-error."

By the same analogy the question might be asked as to whether the individual patient is any better able to judge the competence of a surgeon than is the passenger to select his pilot. In both cases selection must be based upon the judgment of competent examiners rather than incompetent consumers of the specialist's services. Here again the pilot is by circumstances allowed only one serious mistake, while the surgeon may commit many and not even recognize his own errors as such.

Research in factors contributing to postoperative deaths will go on, and succeeding years will undoubtedly bring many more advances to add to those already made. However, these technics will only be applied successfully by the surgeon who has not only been subjected to a long and disciplined training, but is also well enough educated in physiology and biochemistry to keep pace with the derangements which his more and more radical operations impose, and whose conscience requires him to give his best attention to the needs of each and every patient coming within his sphere of responsibility.

JOHN S. LOCKWOOD.

EDITORIAL ADDRESS

Original typed manuscripts and illustrations submitted to this Journal should be forwarded prepaid, at the author's risk, to the Chairman of the Editorial Board of the ANNALS OF SURGERY.

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BOOK REVIEWS

THE THYROID AND ITS DISEASES, by James H. Means, M.D., Professor of Clinical Medicine, Harvard Univ., and Chief of Medical Services, Mass. General Hosp. 2nd Edition. 1948. 571 pages. Philadelphia, J. B. Lippincott Company.

This is a fine medical monograph. It covers in an orderly, superbly arranged manner the entire field of the thyroid and most of its relations with other parts of the body. With the same clear simple style that has always characterized Doctor Means' lectures, the volume traces the subject from the embryologic and phylogenetic development of the gland through the historical and contemporary evidence regarding the nature and action of its hormone, its interrelationships with other endocrine organs, hypothyroidism, hyperthyroidism, nodular goiters and thyroiditis in their various forms. It covers available experience in the use of antithyroid drugs and in the use of radioactive iodine. Coming from the clinic in which the latter material received its first clinical trial it may be regarded as especially authoritative on this subject.

The chapters on pathology by Dr. Rulon W. Rawson and the chapters on surgery by Dr. Oliver Cope are likewise excellent and enhance the value of the book.

Throughout the work the conclusions show the penetrating mind and well balanced judgment of a great clinician. We are fortunate in having this remarkable presentation of Doctor Means' accumulated information and experience in the field of his major interest.

J. E. RHODES, M.D.

SURGICAL PATHOLOGY by Peter A. Herbut, Lea and Febiger, Philadelphia, 1948.

The author has undertaken an impossible task because in so small a volume it is obvious that the field cannot be covered. However, there is a surprising amount of information and the illustrations are, for the most part, excellent and well selected. The effort to correlate the clinical and pathological findings, and in particular, the diagnosis, treatment and prognosis, makes the book easy reading. The references at the end of each chapter in a large part make up for the necessary omissions in such an abbreviated text. This would make it, presumably, a valuable book for the surgeon not in constant contact with a laboratory of surgical pathology.

The greatest defect, which is partly born of the necessity for condensation, but not wholly, is the dogmatic manner in which the material is presented. There are some errors in *fact* some of which are quite striking, such as under carcinoma of the thyroid, the statement that "symptoms of thyrotoxicosis are present in from 13 to 34 per cent of the cases." The errors seemed to be chiefly in the clinical discussion. Nevertheless, they constitute a drawback, particularly when so categorically stated.

The volume could be used by students preferably as a quick reference rather than as a text. It certainly contains a wealth of material and considerable effort has been made by the author to indicate the frequency and the clinical importance of the lesions under discussion.

There are some omissions, notably the pathology of the adrenal, the peripheral nervous system—the author has deliberately omitted the brain and spinal cord—and some neoplasms, as for example, chordoma.

The author is to be congratulated for a current and working handbook of surgical pathology.

VIRGINIA KNEELAND FRANTZ, M.D.